Courtney M. Price
Vice President
CHEMSTAR

American Chemistry Council Good Chemistry Makes It Possible

December 20, 2001

Ms. Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

2001 DEC 21 PM 2:21
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Attn: Chemical Right-to-Know Program Consortium No.

Dear Governor Whitman:

It is my pleasure to submit the Test Plan documents for the Cationics Task Group of the American Chemistry Council's (ACC) Fatty Nitrogen Derivatives (FND) Panel. The Cationics Test Plan compromises five documents:

(1) Robust Summaries of studies and data pertinent to SIDS endpoints (Appendix A);
(2) A Data Assessment Report describing the adequacy and scope of existing data and any further data to be generated;
(3) A Test Plan outlining the proposals to address further data needs;
(4) An index of Government Review documents, of CAS No. 68424-85-1 and CAS No. 7173-51-5; and
(5) Government Review documents of CAS No. 68424-85-1 and CAS No. 7173-51-5 (Appendix B).

Please note that this Test Plan does not include the chemical identified by CAS No. 72749-55-4 which had been initially sponsored by the ACC FND Cationics Task Group but which now is sponsored by the ACC FND Amides Task Group.

Please direct inquiries regarding this letter to Sonny Maher who is the Fatty Nitrogen Derivatives Panel Manager. He can be reached at 703/741-5605 or via e-mail at Sonny_Maher@americanchemistry.com.

Sincerely yours,

Attachment

cc: Cationics Task Group Members
Charles Auer, EPA
Steven Russell, ACC
Jim Keith, ACC

AR201-13407A

Fatty Nitrogen Derived Cationics Category High Production Volume (HPV) Chemicals Challenge

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Test Plan

Prepared for:

American Chemistry Council
Fatty Nitrogen Derivatives Panel
Cationics Task Group

Prepared by:

Toxicology/Regulatory Services, Inc.

December 13, 2001

Fatty Nitrogen Derived Cationics Category
High Production Volume (HPV) Chemicals Challenge
Test Plan

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Fatty Nitrogen Derived Cationics Category
High Production Volume (HPV) Chemicals Challenge
Test Plan

This document provides the Test Plan for the Fatty Nitrogen Derived Cationics Category.

Definition of Fatty Nitrogen Derived (FND) Cationics Structure-Based Chemical Category

The FND Cationics Category is comprised of 13 separate quaternary ammonium compounds (quats) with unique Chemical Abstracts Service Registry Numbers (CAS RNs; see Text Table A). The chemicals in the FND Cationics Category consist of the following:

Five mono-alkyl chain quats (CAS RNs 112-00-5, 112-02-7, 8030-78-2, 112-03-8 and 68607-29-4); seven di-alkyl chain quats (CAS RNs 61789-77-3, 68391-05-9, 68002-59-5, 68783-78-8, 68002-58-4, 61789-80-8 and 61789-81-9); and one tri-alkyl chain quat (CAS RN 67784-77-4).

In addition, three non-HPV chemicals, which are structurally closely-related to the FND Cationics Category, were identified to provide supplemental data for the category. These supporting chemicals consist of a tri-alkyl chain quat (tricetylmethyl ammonium chloride, i.e. TMAC; CAS RN 52467-63-7), a di-alkyl chain quat (didecyldimethylammonium chloride; i.e. DDAC; CAS RN 7173-51-5) and a benzyl mono-alkyl chain quat (Alkyl (C12-16) dimethylbenzylammonium chloride; i.e. ADBAC; CAS RN 68424-85-1), with similar toxicologic properties to DDAC. Although full reports for DDAC and ADBAC could not be obtained by the FND Cationics HPV Task Group, and therefore, Robust Summaries could not be prepared, official government reviews (U. S. EPA Data Evaluation Reviews) of the toxicity, environmental fate and ecotoxicity studies for these chemicals were available and are considered reliable to support fulfilling HPV endpoints for the FND Cationics Category (U. S. EPA Data Evaluation Reports; Environment Canada, 1998 and Ministry of Environment, Lands, and Parks, 1992; see Appendix B).

U. S. EPA clustered quaternary ammonium compounds into four groups for the purpose of toxicology testing needed for reregistration under FIFRA (U. S. EPA, 1988). Although the FND Cationics Category chemicals are not part of this FIFRA reregistration, based on their structures, they all fit into Group I of the EPA clustering scheme. EPA designated DDAC as the representative member of Group I, meaning that data developed for this chemical would be representative for the other quats in the Group. ADBAC was designated by EPA as representative of a second group, Group II, of quaternary ammonium compounds, those with a benzyl substituent. For the purpose of determining environmental toxicity, DDAC and ADBAC remained the representative members of their respective groups (U. S. EPA, 1993). It was determined during the testing for reregistration under FIFRA that, despite their structural diversity, the quats included in EPA Groups I and II all had similar toxicological, environmental fate and ecotoxicological profiles. The FND Cationics Category chemicals appropriately fit into the EPA scheme for Group 1, and the inclusion of data for DDAC in support of the category is appropriate. Although the FND Cationics Category chemicals do not include benzene substituted quaternary amines, the similar toxicological profile for ADBAC and DDAC warrant the inclusion of ADBAC as a second supporting chemical for the category.

The FND Cationics Category chemicals and supporting non-HPV chemicals are identified in the following table:

Text Table A: CAS Registry Numbers and Chemical Names

CAS RN	Chemical Name
112-00-5	Ammonium, dodecyltrimethyl-, chloride
112-02-7	Ammonium, hexadecyltrimethyl-, chloride
8030-78-2	Quaternary ammonium compounds, trimethyltallow alkyl, chlorides
112-03-8	Trimethyloctadecylammonium chloride
7173-51-5 non-HPV	*Didecyldimethylammonium chloride (DDAC)*
61789-77-3	Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides
68391-05-9	Quaternary ammonium compounds, di-C12-18-alkyldimethyl, chlorides
68002-59-5	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, chlorides
68783-78-8	Quaternary ammonium compounds, dimethylditallow alkyl, chlorides
68002-58-4	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, Me sulfates
61789-80-8	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride
61789-81-9	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, Me sulfates
52467-63-7 non-HPV	*1-Hexadecanaminium, N, N-dihexadecyl-N-methyl-, chloride (Tricetylmethyl ammonium chloride, TMAC)*
67784-77-4	Quaternary ammonium compounds, bis(hydroxyethyl)methyltallow alkyl, chlorides
68607-29-4	Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichloride
68424-85-1 non-HPV	*Alkyl (C12-16) dimethylbenzylammonium chloride (ADBAC)*

Evaluation of Matrix Data Patterns – Reliable Data and QSAR Predictions

Physical/Chemical Properties

Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

Melting Point, Boiling Point and Vapor Pressure: Melting point and boiling point data as predictors of environmental or toxicological behavior for chemicals such as the FND Cationics Category chemicals are of minimal value. The QSAR estimates for melting point and boiling point appear to provide values higher than would be expected. A measured boiling point for TMAC was considered to be confounded by impurities. Overall, the measured and modeled values are adequate for defining melting and boiling points for the FND Cationics Category chemicals.

As expected for molecules of this size, model predictions for the chemicals with definable structures indicate they are nonvolatile. A measured vapor pressure value suggesting TMAC is volatile was considered to be confounded by impurities. Overall, the available information is adequate to meet HPV requirements.

> **Additional Data:** No additional data are proposed for the melting point, boiling point and vapor pressure endpoints (see Table 1).

Octanol/Water Partition Coefficient (K_{ow}) and Water Solubility: Predicted or measured K_{ow} values are of limited practical use for cationic substances to estimate their physical properties or behavior in the environment. An inherent property of cationic surfactants is that they accumulate at the interface between two phases. Thus, the accurate measurement of the K_{ow} for any surfactant is difficult. Even if such measurements were made accurately, the K_{ow} is not an appropriate hydrophobicity parameter for reliably predicting environmental behavior because cationic substances in the environment instantaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments and with dissolved humic substances in surface waters.

The water solubility for the FND Cationics Category appears to be influenced by substituent groups, chain lengths and molecular weight. However, due to the physical/chemical properties of these surfactants described above, water solubility values for the FND Cationics Category chemicals are of limited value in predicting their environmental fate and toxicity. Thus, the available modeled and measured data for the FND Cationics Category chemicals and additional chemicals are considered adequate to meet the requirements of the HPV program.

> **Additional Data:** No additional data are proposed for the partition coefficient or water solubility endpoints (see Table 1).

Environmental Fate and Ecotoxicity

Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

Photodegradation, Water Stability and Transport and Distribution: Due to the extremely low volatility of the FND Cationics Category chemicals, atmospheric photodegradation estimates are of no practical value. However, photodegradation was predicted for three of the FND Cationics Category chemicals and the three non-HPV chemicals. These predictions indicate that these chemicals would be expected to degrade relatively rapidly upon exposure to light ($t_{1/2}$ values ranging from approximately 2.8 to 5.9 hours). In addition, a measurement for CAS RN 61789-80-8 adsorbed to silica indicated some evidence of photodegradation.

The water stability of these chemicals could not be modeled since the structures of the FND Cationics Category chemicals did not meet the requirements of the model's database. Due to the surfactant properties of the FND Cationics Category chemicals, water stability estimates are of little practical value. The measured data available from a hydrolysis test with DDAC indicate that the test substance was stable in water for 30 days at pHs of 5, 7 and 9. Similar results would be expected for the FND Cationics Category chemicals.

The fugacity model (Level III) predictions for transport and distribution are consistent with the model dependency on K_{ow} and water solubility. Thus, for the chemicals with lower K_{ow} estimates and higher water solubility estimates, the model predicts high distribution into water. Conversely, for chemicals with higher K_{ow} and lower water solubility predictions, the model predicts high distribution to sediment.

> **Additional Data:** Due to the extremely low volatility of the FND Cationics Category chemicals, atmospheric photodegradation estimates are of no practical value and no testing is proposed. In addition, due to the surfactant properties of the FND Cationics Category chemicals, water stability estimates are of little practical value and no testing is proposed. For purposes of the HPV program, model predictions available for chemicals with definable structures are adequate to describe distribution and transport for the FND Cationics Category chemicals and no additional data development is proposed (see Table 2).

Biodegradability: There are adequate measured data across the FND Cationics Category to allow the conclusion that these chemicals are biodegradable although tests are frequently confounded by adsorption phenomena. For the non-HPV chemical, ADBAC, the most recent review by Environment Canada (1998; Appendix B) concludes, "It is not persistent in the water column; movement to the solid phase and microbial degradation are expected to be the main routes of dissipation." This conclusion is consistent with the information available for the FND Cationics Category chemicals as well.

> **Additional Data:** No additional data development is proposed for the biodegradation endpoint (see Table 2).

Aquatic Toxicity: The reliable data for acute toxicity to aquatic organisms indicate that the FND Cationics Category chemicals, like surfactants in general, may adversely affect some species (LC_{50} and EC_{50} values as low as 0.07 mg/l). Chronic toxicity to fish and invertebrate species varied considerably, with NOECs ranging from 4.15 µg/l to 12.7 mg/l. The numerous studies of aquatic toxicity, many of which were conducted in natural waters with and without added effluents, indicate that the source and composition of the test water dramatically affects the toxicity of the test substance. These results are consistent with the known behavior of these materials in the environment. Cationic substances in the environment instantaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and with dissolved humic substances in surface waters. This complexation behavior results in reduced bioavailability in actual environmental conditions that is not adequately represented by standard laboratory assays and/or predictions by EPIWIN SAR models. Thus the extreme variability of the measured values is predictable. Further, as would be anticipated, the modeling programs were inconsistent in their accuracy for aquatic toxicity endpoints with some values similar to measured or expected and others divergent. Overall, there are substantial aquatic toxicity experimental data for the FND Cationics Category chemicals and these data are similar to a number of published values for similar quaternary ammonium compounds (Boethling and Lynch, 1992).

The values for toxicity to aquatic plants for two of the chemicals (CAS RNs 68783-78-8 and 61789-80-8) in the FND Cationics Category are consistent with 1) published data for similar quaternary ammonium compounds (Boethling and Lynch, 1992), 2) the value for the structurally-related non-HPV chemical, DDAC (Ministry of Environment, Lands, and Parks, 1992), and 3) the acute effects on other aquatic organisms. Toxicity to aquatic plants could not be modeled using ECOSAR for the chemicals in the FND Cationics Category. Values for toxicity to aquatic plants for the non-HPV chemical, TMAC, were similar to other reported values.

> **Additional Data:** Based on the close similarity of FND Cationics Category aquatic toxicity data (measured and modeled) to those known for other quaternary ammonium compounds as well as the confounding potential of adsorption to environmental substances, additional acute toxicity testing of aquatic animals and plants will not provide new data of consequence to better understand the aquatic toxicity of cationic surfactants. Therefore, no additional data development is proposed (see Table 2).

Human Health-Related Data

Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

Acute Toxicity: Acute oral toxicity studies were available for nine of the FND Cationics Category chemicals, as well as for the two non-HPV chemicals, DDAC and ADBAC. These studies indicate a range of acute oral toxicity from approximately 200 to > 2000 mg/kg. An oral LD_{50} of > 16.3 g/kg was found for the high molecular weight, non-HPV chemical, TMAC.

Repeated Dose and Reproductive Toxicity: The available data for four FND Cationics Category chemicals support the assessment of repeated dose toxicity; two of these studies meet the SIDS/HPV requirements for reproductive screening. For purposes of the HPV program, the repeat dose study for the non-HPV chemical, TMAC, as well as the extensive repeat dose and reproductive testing of the two non-HPV chemicals, DDAC and ADBAC, adequately support the evaluation of the FND Cationics Category chemicals.

Genetic Toxicity *in vitro*: Mutagenicity data with some limitations (several of the existing studies do not meet current testing guidelines for the number of strains to be tested) are available for the HPV chemicals. The available data indicate that the FND Cationics Category chemicals are unlikely to be mutagenic. The conclusion of a lack of mutagenicity and clastogenicity for FND Cationics Category chemicals is supported robustly by the full complement of studies available for the three non-HPV chemicals, including a negative *in vivo* mouse micronucleus assay for ADBAC (see Appendix B) and a negative *in vivo* chromosomal aberration assay for TMAC (see Appendix A).

Developmental Toxicity: The data available from tests for developmental toxicity for five FND Cationic Category chemicals and the two non-HPV chemicals, DDAC and ADBAC, indicate that these chemicals are neither embryo/fetal toxicants nor teratogens. For purposes of the HPV program, the available studies adequately support the evaluation of the FND Cationics Category chemicals.

> **Additional Data:** For HPV program purposes, the available data are sufficient for the evaluation of the FND Cationics Category chemicals. Therefore, no additional data development is proposed for the acute toxicity, repeated dose and reproductive toxicity, genetic toxicity *in vitro* or developmental toxicity endpoints (see Table 3).

References

Boethling, R. S. and D. G. Lynch. 1992. Quaternary Ammonium Surfactants. *Handbook of Environ. Chem.* 3: 145-177.

Environment Canada. 1998. Water Quality Guideline for the Protection of Freshwater Aquatic Life for Didecyl Dimethyl Ammonium Chloride (DDAC). Guidelines and Standards Division, Science Policy and Environment Quality Branch, Environment Canada, Hull, Quebec, December 1998.

Ministry of Environment, Lands, and Parks. 1992. "A Review of the Environmental Impact and Toxic Effects of DDAC." Victoria, British Columbia.

U. S. EPA. 1988. PR Notice 88 – 2. Notice to Producers, Formulators, Distributors and Registrants: Clustering of Quaternary Ammonium compounds

U. S. EPA. 1993. Memorandum: OPPTS' Structure Activity Clustering of OPP's Quaternary Ammonium Compounds for Environmental Toxicity.

Table 1. Proposed Test Plan for American Chemistry Council FND Cationics Category
Physical/Chemical Properties

CAS RN	Melting Point	Boiling Point	Vapor Pressure	Partition Coefficient (log K_{ow})	Water Solubility
112-00-5	A	A	A	A	A
112-02-7	A	A	A	A	A
8030-78-2	C	C	C	C	C
112-03-8	A	A	A	A	A
7173-51-5 non-HPV	*A*	*A*	*A*	*A*	*A*
61789-77-3	C	C	C	C	C
68391-05-9	C	C	C	C	C
68002-59-5	C	C	C	C	C
68783-78-8	C	C	C	C	C
68002-58-4	C	C	C	C	C
61789-80-8	A	C	C	C	A
61789-81-9	C	C	C	C	C
52467-63-7 non-HPV	*A*	*A*	*A*	*A*	*A*
67784-77-4	C	C	C	C	C
68607-29-4	C	C	C	C	C
68424-85-1 non-HPV	*A*	*A*	*A*	*A*	*A*

Note: Shaded areas represent adequate reliable data, adequate model data.
CAS RN and data in italics are for additional chemicals [non-HPV].
A = Adequate reliable data or model data exist.
C = Endpoint fulfilled by category read-across from existing data.

Table 2. Proposed Test Plan for American Chemistry Council FND Cationics Category Environmental Fate and Ecotoxicity[a]

CAS RN	Photodegradation	Stability in Water	Transport & Distribution	Biodegradation	Acute Tox. to Fish	Acute Tox. to Invertebrates	Toxicity to Aquatic Plants
112-00-5	A	C	A	A	A	A	C
112-02-7	A	C	A	A	A	A	C
8030-78-2	C	C	C	A	C	A	C
112-03-8	A	C	A	A	A	A	C
7173-51-5 non-HPV	*A*	*A*	*A*	*A*	*A*	*A*	*A*
61789-77-3	C	C	C	A	C	C	C
68391-05-9	C	C	C	C	C	C	C
68002-59-5	C	C	C	C	C	C	C
68783-78-8	C	C	C	C	A	A	A
68002-58-4	C	C	C	C	C	C	C
61789-80-8	A	C	C	A	A	A	A
61789-81-9	C	C	C	C	C	C	C
52467-63-7 non-HPV	*A*	*C*	*A*	*A*	*A*	*A*	*A*
67784-77-4	C	C	C	C	C	C	C
68607-29-4	C	C	C	A	C	C	C
68424-85-1 non-HPV	*A*	*C*	*A*	*A*	*A*	*A*	*C*

Note: Shaded areas represent adequate reliable data or adequate model data
CAS RN and data in italics are for additional chemicals [non-HPV].
A = Adequate reliable data or model data exist.
C = Endpoint fulfilled by category read-across from existing or proposed test data.
[a] In addition to the SIDS/HPV endpoints for aquatic toxicity, chronic toxicity studies exist, are discussed in the Assessment of Data Availability, and are included in the Robust Summaries in Appendix A.

Table 3. Proposed Test Plan for American Chemistry Council FND Cationics Category Human Health-Related Data

CAS RN	Acute Oral Toxicity	Acute Inhalation Toxicity	Acute Dermal Toxicity	Repeated Dose Toxicity NOEL	Genetic Toxicity *In vitro*	Toxicity to Reproduction	Developmental Toxicity
112-00-5	A	C	C	C	A	C	A
112-02-7	A	C	A	A	A	C	A
8030-78-2	A	C	A	C	A	C	C
112-03-8	A	C	C	C	A	C	A
7173-51-5 non-HPV	*A*	*C*	*A*	*A*	*A*	*A*	*A*
61789-77-3	A	C	C	C	A	C	C
68391-05-9	A	C	C	A	C	C	C
68002-59-5	C	C	C	C	C	C	C
68783-78-8	A	C	C	C	A	C	A
68002-58-4	C	C	C	C	C	C	C
61789-80-8	A	A	C	A	C	A	C
61789-81-9	C	C	C	A	C	A	A
52467-63-7 non-HPV	*A*	*C*	*A*	*A*	*A*	*C*	*C*
67784-77-4	C	C	C	C	C	C	C
68607-29-4	A	C	C	C	C	C	C
68424-85-1 non-HPV	*C*	*C*	*C*	*A*	*A*	*A*	*A*

Note: Shaded areas represent adequate reliable data.
CAS RN and data in italics are for additional chemicals [non-HPV].
Reliable data for acute toxicity by any of the three routes of exposure are considered adequate under the EPA HPV Challenge Program.
A = Adequate reliable data exist.
C = Endpoint fulfilled by category read-across from existing or proposed test data.

Fatty Nitrogen Derived Cationics Category
High Production Volume (HPV)
Chemicals Challenge

Assessment of Data Availability

Prepared for:

American Chemistry Council
Fatty Nitrogen Derivatives Panel
Cationics Task Group

Prepared by:

Toxicology/Regulatory Services, Inc.

December 13, 2001

Fatty Nitrogen Derived Cationics Category
High Production Volume (HPV) Chemicals Challenge
Assessment of Data Availability

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Appendix A

Appendix B

Fatty Nitrogen Derived Cationics Category
High Production Volume (HPV) Chemicals Challenge
Assessment of Data Availability

Introduction

Surfactants have a long history of safe use and have been studied extensively for environmental fate and effects and human health effects. The Fatty Nitrogen Derived (FND) Cationics Category chemicals are similar to the surfactants class in general as to physical/chemical properties, environmental fate and toxicity. Some typical applications of FND Cationics Category chemicals are: fabric softeners, multifunctional liquid laundry detergents, antistatic sprays, germicides, deodorizers, emulsifiers, hair-care preparations, and industrial lubricants and corrosion inhibitors (Boethling and Lynch, 1992).

Of the three non-HPV chemicals included in the FND Cationics Category, DDAC and ADBAC are FIFRA registered antimicrobial chemicals with germicidal, fungicidal and algicidal activity. They are used extensively as bactericides, fungicides, sanitizers, deodorants and disinfectants in the restaurant, dairy, food, laundry and medical industries (Ministry of Environment, Lands, and Parks, 1992). The third non-HPV chemical included in the FND Cationics Category, TMAC, is a trialkyl quat of similar use as the HPV chemicals.

The low order of toxicity indicates that the use of FND Cationics Category chemicals does not pose a significant hazard to human health.

Definition of Fatty Nitrogen Derived (FND) Cationics Structure-Based Chemical Category

The FND Cationics Category is comprised of 13 separate quaternary ammonium compounds (quats) with unique Chemical Abstracts Service Registry Numbers (CAS RNs; see Text Table A). The chemicals in the FND Cationics Category consist of the following:

Five mono-alkyl chain quats (CAS RNs 112-00-5, 112-02-7, 8030-78-2, 112-03-8 and 68607-29-4); seven di-alkyl chain quats (CAS RNs 61789-77-3, 68391-05-9, 68002-59-5, 68783-78-8, 68002-58-4, 61789-80-8 and 61789-81-9); and one tri-alkyl chain quat (CAS RN 67784-77-4).

In addition, three non-HPV chemicals, which are structurally closely-related to the FND Cationics Category, were identified to provide supplemental data for the category. These supporting chemicals consist of a tri-alkyl chain quat (tricetylmethyl ammonium chloride, i.e. TMAC; CAS RN 52467-63-7), a di-alkyl chain quat (didecyldimethylammonium chloride, i.e. DDAC; CAS RN 7173-51-5) and a benzyl mono-alkyl chain quat (Alkyl (C12-16) dimethylbenzylammonium chloride; i.e. ADBAC; CAS RN 68424-85-1), with similar toxicologic properties to DDAC. Although full reports for DDAC and ADBAC could not be obtained by the FND Cationics HPV Task Group, and therefore, Robust Summaries could not be prepared, official government reviews (U. S. EPA Data Evaluation Records for ADBAC and summaries for DDAC) of the toxicity, environmental fate and ecotoxicity studies for these chemicals were available and are considered reliable to support fulfilling HPV endpoints for the

FND Cationics Category (U. S. EPA Data Evaluation Report [DERs]; Environment Canada 1998; and Ministry of Environment, Lands, and Parks, 1992; see Appendix B).

U. S. EPA clustered quaternary ammonium compounds into four groups for the purpose of toxicology testing needed for reregistration under FIFRA (U. S. EPA, 1988). Although the FND Cationics Category chemicals are not part of this FIFRA reregistration, based on their structures, they all fit into Group I of the EPA clustering scheme. EPA designated DDAC as the representative member of Group I, meaning that data developed for this chemical would be representative for the other quats in the Group. ADBAC was designated by EPA as representative of a second group, Group II, of quaternary ammonium compounds, those with a benzyl substituent. For the purpose of determining environmental toxicity, DDAC and ADBAC remained the representative members of their respective groups (U.S. EPA, 1993). It was determined during the testing for reregistration under FIFRA that, despite their structural diversity, the quats included in EPA Groups I and II all had similar toxicological, environmental fate and ecotoxicological profiles. The FND Cationics Category chemicals appropriately fit into the EPA scheme for Group 1, and the inclusion of data for DDAC in support of the category is appropriate. Although the FND Cationics Category chemicals do not include benzene substituted quaternary amines, the similar toxicological profile for ADBAC and DDAC warrant the inclusion of ADBAC as a second supporting chemical for the category.

The FND Cationics Category chemicals and supporting non-HPV chemicals are identified in the following table:

Text Table A: CAS Registry Numbers and Chemical Names

CAS RN	Chemical Name
112-00-5	Ammonium, dodecyltrimethyl-, chloride
112-02-7	Ammonium, hexadecyltrimethyl-, chloride
8030-78-2	Quaternary ammonium compounds, trimethyltallow alkyl, chlorides
112-03-8	Trimethyloctadecylammonium chloride
7173-51-5 non-HPV	*Didecyldimethylammonium chloride (DDAC)*
61789-77-3	Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides
68391-05-9	Quaternary ammonium compounds, di-C12-18-alkyldimethyl, chlorides
68002-59-5	Quaternary ammonium compounds,di-C14-18-alkyldimethyl, chlorides
68783-78-8	Quaternary ammonium compounds, dimethylditallow alkyl, chlorides
68002-58-4	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, Me sulfates
61789-80-8	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride
61789-81-9	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, Me sulfates
52467-63-7 non-HPV	*1-Hexadecanaminium, N, N-dihexadecyl-N-methyl-, chloride (Tricetylmethyl ammonium chloride, TMAC)*
67784-77-4	Quaternary ammonium compounds, bis(hydroxyethyl)methyltallow alkyl, chlorides
68607-29-4	Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichloride
68424-85-1 non-HPV	*Alkyl (C12-16) dimethylbenzylammonium chloride (ADBAC)*

Structural Information for the FND Cationics Category and Supplemental Chemicals

The following table presents the molecular formula and molecular weight data for the chemicals with defined structures or structures for which average chain lengths can be determined. The structures for these and the remaining chemicals in the FND Cationics Category and non-HPV chemicals are provided in Table 1.

Text Table B: Molecular Formula and Molecular Weight of Chemicals with Defined Structures

CAS RN	Name	Molecular Formula	Molecular Weight
112-00-5	Ammonium, dodecyltrimethyl-, chloride	$C_{15}H_{34}NCl$	263
112-02-7	Ammonium, hexadecyltrimethyl-, chloride	$C_{19}H_{42}NCl$	319
112-03-8	Trimethyloctadecylammonium chloride	$C_{21}H_{46}NCl$	347
7173-51-5	*Didecyldimethylammonium chloride*	*$C_{22}H_{48}NCl$*	*361*
68391-05-9	Quaternary ammonium compounds, di-C12-18-alkyldimethyl, chlorides	$C_{32}H_{74}NCl$ [a]	507
68002-59-5	Quaternary ammonium compounds,di-C14-18-alkyldimethyl, chlorides	$C_{34}H_{78}NCl$ [b]	535
68002-58-4	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, Me sulfates	$C_{33}H_{77}NSO_4$ [a]	583
52467-63-7	*Tricetylmethyl ammonium chloride*	$C_{49}H_{102}NCl$	739
68424-85-1	*Alkyl (C12-16) dimethylbenzylammonium chloride*	$C_{23}H_{45}NCl$ [c]	370

Entries in italics are non-HPV chemicals
[a] Based on average chain length = 15
[b] Based on average chain length = 16
[c] Based on average chain length = 14

Rationale for the FND Cationics Structure-Based Chemical Category

The FND Cationics Category surfactants are included as a single HPV chemical category based on the following generalities:

- Structural and functional similarities of cationic surfactants;
- Similar measured and modeled physical properties such as melting point, boiling point, vapor pressure, partition coefficient (log K_{ow}) and water solubility;
- Similar biodegradability;
- Aquatic toxicity observed at low concentrations, as observed with surfactants in general;
- Moderate to negligible mammalian toxicity;

- Similar uses and disposition patterns in the environment; and
- Chemicals of the Category fitting into a "clustering" group established by EPA during the reregistration of quaternary ammonium compounds used as antimicrobials under FIFRA.

Available Data to Fulfill HPV Screening Information Data Set (SIDS) Endpoints

Approach to Evaluate the Database for the FND Cationics Category

The following approach was used to obtain and analyze data relevant to the assessment of the FND Cationics Category.

1. The chemical names and CAS RNs of the 13 HPV FND Cationics Category chemicals supported by the American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group (Task Group) were provided.
2. The names of three non-HPV chemicals and their CAS registry numbers, structurally and functionally similar to the members of the proposed FND Cationics Category, were added.
3. Available published and unpublished reports were obtained from the members of Task Group and other chemical industry companies; they were organized and reviewed to identify studies that could fulfill SIDS endpoints.
4. Pertinent databases[1] were searched and all relevant reports were obtained to establish the full extent and nature of the published literature for the 13 FND Cationics Category and three non-HPV supplemental chemicals.
5. Each of the reports obtained was reviewed (except government reports for DDAC and ADBAC, which were considered to be reliable *a priori*) to determine adequacy according to EPA criteria and reliability according to Klimisch *et al.* (1997).
6. Robust summaries were prepared for each report with Klimisch scores of 1 or 2, according to the guidelines proposed by the EPA (U. S. EPA, 1999a) for each study type.
7. Estimates for physical/chemical properties, environmental fate and ecotoxicity values were developed by using appropriate Quantitative Structure Activity Relationships (QSARs).
8. Fugacity modeling was performed to estimate transport and distribution into environmental compartments for the HPV and non-HPV chemicals.

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[1] Databases include ChemIDplus HSDB (Hazardous Substances Data Bank), IRIS (Integrated Risk Information System), CCRIS (Chemical Carcinogenesis Research Information System), GENE-TOX, EMIC (Environmental Mutagen Information Center), DART/ETIC (Developmental and Reproductive Toxicology and Environmental Teratology Information Center), MEDLINE, TOXLINE, RTECS (Registry of Toxic Effects of Chemical Substances),TSCATS (Toxic Substances Control Act Test Submissions),IUCLID, 1996 (International Uniform Chemical Information Database)

Use of Structure Activity Relationships for the FND Cationics Category

Approaches recommended in the EPA document on the use of structure activity relationship (SAR) in the HPV Chemicals Challenge Program were employed in the assessment of the FND Cationics Category (U. S. EPA, 1999b). Several models were employed to support the review and assessment of the FND Cationics Category chemicals. The models included several based on structure-activity relationships (SAR), as well as Mackay-type fugacity-based modeling. The SAR models for physical properties were used to estimate boiling point, melting point, aqueous solubility, octanol-water partition coefficient and vapor pressure. Other SAR models were used to estimate hydroxyl radical mediated atmospheric photo-oxidation and biodegradation potential. SAR models also were used to obtain conservative estimates of acute toxicity to aquatic organisms.

Common Features of the Models

All of the models (except the Mackay-type models) require the input of a molecular structure to perform the calculations. The structure must be entered into the model in the form of a SMILES (Simplified Molecular Input Line Entry System) notation or string. SMILES is a chemical notation system used to represent a molecular structure by a linear string of symbols. The SMILES string allows the program to identify the presence or absence of structural features used by the submodels to determine the specific endpoint. The models contain files of structures and SMILES strings for approximately 100,000 compounds, accessible via CAS RNs. SMILES strings cannot be developed for mixtures or chemicals without a single, definable structure.

Estimation of Physical/Chemical Properties

The SAR models for estimating physical properties and abiotic degradation were obtained from Syracuse Research Corporation 2000 (Estimation Programs Interface for Windows, Version 3.05 or EPIWIN v.3.05). The models were used to calculate melting point, boiling point, vapor pressure (submodel MPBPVP), octanol-water partition coefficient (K_{ow}) (submodel KOWWIN) and aqueous solubility (submodel WSKOWWIN). The calculation procedures are described in the program guidance and are adapted from standard procedures based on analysis of key structural features (Meylan and Howard, 1999a, b and c).

Estimation of Environmental Fate Properties

Atmospheric photo-oxidation potential was estimated using the submodel AOPWIN (Meylan and Howard, 2000a). The estimation methods employed by AOPWIN are based on the SAR methods developed by Dr. Roger Atkinson and co-workers (Meylan and Howard, 2000a). The SAR methods rely on structural features of the subject chemical. The model calculates a second-order rate constant with units of cm^3/molecules-sec. Photodegradation based on atmospheric photo-oxidation is in turn based on the rate of reaction (cm^3/molecules-sec) with hydroxyl radicals (HO•), assuming first-order kinetics and an HO• concentration of 1.5 E + 6 molecules/cm^3 and 12 hours of daylight. Pseudo first-order half-lives ($t_{1/2}$) were then calculated as follows: $t_{1/2} = 0.693/[(k_{phot} \times HO\bullet) \times (12\text{-hr}/24\text{-hr})]$.

The database that supports the modeling of water stability provides only for neutral organic compounds that have structures that can be hydrolyzed. Therefore, no model estimates for hydrolytic stability are available since the FND Cationics Category chemicals do not have the necessary characteristics.

Biodegradation potential was estimated using the submodel BIOWIN (Meylan and Howard, 2000b). BIOWIN estimates the probability for the rapid aerobic biodegradation of an organic chemical in the presence of mixed populations of environmental micro-organisms. Estimates are based on fragment constants that were developed using multiple linear and nonlinear regression analyses (Meylan and Howard, 2000b). BIOWIN uses the probabilities to estimate a potential pseudo first-order half-life for aerobic biodegradation of the subject chemical in surface water, soil and sediment.

Estimation of Environmental Distribution

The Level 3 Mackay-type, fugacity-based models were obtained from the Trent University's Modeling Center. The specific model used was the generic Equilibrium Concentration model (EQC) Level 3, version 1.01. These models are described in Mackay *et al*. (1996a and b). Fugacity-based modeling is based on the "escaping" tendencies of chemicals from one phase to another. For instance, a Henry's Law constant calculated from aqueous solubility and vapor pressure is used to describe the "escape" of a chemical from water to air or vice versa, as equilibrium between the phases is attained. The key physical properties required as input parameters into the model are melting point, vapor pressure, K_{ow} and aqueous solubility. The model also requires estimates of first-order half-lives in the air, water, soil and sediment. An additional key input parameter is loading of the chemical into the environment.

Estimation of Acute Aquatic Toxicity

Models developed by the U. S. Environmental Protection Agency (EPA) were employed to make estimates of acute toxicity to aquatic organisms, specifically to the fathead minnow (*Pimephales promelas*), a commonly tested fish; a water column dwelling invertebrate (*Daphnia magna*); and a commonly tested green alga, *Selenastrum capricornutum*. The models are incorporated in a modeling package called ECOSAR, version 0.99f (U. S. EPA, 2000). ECOSAR may be obtained from the EPA website for the Office of Pollution Prevention and Toxics, Risk Assessment Division. The models calculate inherent toxicity based on structural features and physical properties, mainly the K_{ow} (Meylan and Howard, 1998).

Modeling Information Specific to the FND Cationics Category

When CAS RNs were included in the files of structures, the models described above were used for the FND Cationics Category chemicals and the three non-HPV chemicals. Estimations of physical properties, environmental fate and distribution, and ecotoxicity were not possible for 10 of the 13 HPV chemicals in the FND Cationics Category because they do not have single definable structures and/or were not available in the files of structures of the models. Model predictions were available for the three non-HPV chemicals. As noted above, the ECOSAR models are heavily dependent on calculation of the octanol/water partition coefficient, K_{ow}. Therefore, it is important to note that, for cationic substances, K_{ow} estimation is of limited value in estimating their physical properties or behavior in the environment. An inherent property of cationic surfactants is that they accumulate at the interface between two phases. Thus, the accurate measurement of the K_{ow} for any surfactant is difficult. Even if such measurements were made accurately, the K_{ow} is not an appropriate hydrophobicity parameter for reliably predicting environmental behavior. Cationic substances in the environment instantaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and with dissolved humic substances in surface waters. This complexation behavior results in reduced bioavailability in actual environmental conditions that is not adequately represented by standard laboratory assays and/or predictions by EPIWIN SAR models. The model did not provide estimates of stability in water for this class of chemicals because the model cannot calculate this parameter for chemicals that do not meet the criteria of neutral organic compounds with structures that can be hydrolyzed. Since the FND Cationics Category chemicals are considered to be released into wastewater treatment systems (Boethling and Lynch, 1992) for treatment prior to release into surface water, release to soil and air were considered to be minor avenues of entry for FND Cationics Category chemicals into the environment. Therefore, for fugacity modeling, all input was assumed to be into surface water using the chemical specific parameters to attain estimates of the chemical distributions between environmental compartments. The ECOSAR model has not been developed to provide an estimate of toxicity to aquatic plants for the cationic surfactants.

Availability of Reliable Data for the FND Cationics Category

Robust summaries for SIDS/HPV endpoint studies and other supporting studies with reliable data (according to Klimisch criteria) for the HPV chemicals and tricetylmethyl ammonium chloride (TMAC; non-HPV chemical) are provided in Appendix A and are summarized in Tables 2 through 4. Data for the non-HPV chemicals, DDAC and ADBAC, obtained from U. S. EPA Data Evaluation Reports, Environment Canada (1998) and Ministry of Environment, Lands, and Parks (1992), are included in Appendix B and are summarized in Tables 2 through 4.

Reliable data were available for one HPV chemical (CAS RN 61789-80-8) for melting point and water solubility to meet the physical/chemical properties SIDS/HPV endpoints. Reliable, measured melting point, boiling point, vapor pressure, octanol/water partition coefficient, and water solubility values were available for the non-HPV chemical, TMAC. In addition, Environment Canada (1998) includes partition coefficient and water solubility information for the non-HPV chemical, DDAC.

Reliable data were available for environmental fate and ecotoxicity endpoints as shown in the following table:

Text Table C: Number of Available Reliable Environmental Fate and Ecotoxicity Studies

CAS RN	Photodegradation	Biodegradation	Acute Tox. to Fish	Acute Tox. to Invertebrates	Acute Tox. to Aquatic Plants	Chronic Tox. to Aquatic Species
112-00-5		2	1	2		7
112-02-7		3	1			1
8030-78-2		4		1		1
112-03-8		1	1			
7173-51-5 non-HPV		[a]	[a]	[a]	[a]	
61789-77-3		2				
68391-05-9						
68002-59-5						
68783-78-8			2	6 [b]	2 [b]	3
68002-58-4						
61789-80-8	1	2	4 [b]	1 [b]	1 [b]	
61789-81-9						
52467-63-7 non-HPV		2	1	1	1	2 [c]
67784-77-4						
68607-29-4		1				
68424-85-1 non-HPV			[a]	[a]		[a]

Note: Empty block denotes data were not found or that relevant data were found but judged inadequate.

[a] Data for the non-HPV chemicals DDAC and ADBAC are taken from Ministry of Environment, Lands, and Parks, 1992 and/or Environment Canada, 1998 (DDAC), or U. S. EPA DERs (ADBAC) and are included in Appendix B.

[b] More than one value for different species may be summarized in one Robust Summary (Appendix A).

[c] Includes a bacterial toxicity study

Reliable data were available for human health-related toxicity endpoints as shown in the following table:

Text Table D: Number of Available Reliable Human Health-Related Studies

CAS RN	Acute Oral Tox.	Acute Inhalation Tox.	Acute Dermal Tox.	Repeated Dose Tox.	Genetic Tox.	Toxicity to Reproduction	Developmental Tox.
112-00-5	2				4		1
112-02-7	1		1	1	3		1
8030-78-2	1		2		2		
112-03-8	1				1		1
7173-51-5 non-HPV	*a*		*a*	*a*	*a*	*a*	*a*
61789-77-3	1				1		
68391-05-9	1			1			
68002-59-5							
68783-78-8	1				1		1
68002-58-4							
61789-80-8	2	1		2		1[b]	
61789-81-9				1		1[b]	1
52467-63-7 non-HPV	1		1	1	2		
67784-77-4							
68607-29-4	1						
68424-85-1 non-HPV				*a*	*a*	*a*	*a*

Note: Empty block denotes data were not found or that relevant data were found but judged inadequate.
a Data for the non-HPV chemicals DDAC and ADBAC are taken from Ministry of Environment, Lands, and Parks, 1992 and/or Environment Canada, 1998 (DDAC), or U. S. EPA DERs (ADBAC) and are included in Appendix B.
b Repeated dose toxicity study meets the SIDS requirement for a reproductive screen (i.e. histological evaluation of reproductive organs).

Physical/Chemical Properties QSAR Estimates and Correlation to Reliable Data

The available reliable data and QSAR estimates for physical/chemical properties of the FND Cationics Category chemicals are presented in Table 2. Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

As described above, the physical/chemical property estimation program, EPIWIN 1.c. 3.05, was used to derive estimates. The EPIWIN estimates must be interpreted with a great deal of professional judgment.

The QSAR estimates are based on structure and, therefore, can be made only for substances for which a structure can be defined. Thus, a complete set of model data was generated for three of the 13 HPV chemicals with discrete structures (CAS RNs 112-00-5, 112-02-7 and 112-03-8). In addition, model predictions for physical/chemical properties were generated for the three non-

HPV chemicals, DDAC, TMAC and ADBAC. The compositional variability of the chemicals without definable structures also makes the experimental measurement of physical/chemical properties of these chemicals of minimal practical value for prediction of their environmental behavior or toxicological properties. Therefore, the chemicals in the FND Cationics Category without defined structures are best supported by the other chemicals in the category for which the properties can be measured and/or modeled.

The available data for physical/chemical properties are summarized below:

EPIWIN predicted melting points ranged from 182 to 350 ºC. The available measured value, for CAS RN 61789-80-8 was 50 to 60 ºC, but this chemical could not be modeled to allow comparison of measured to modeled data. For the non-HPV chemical, TMAC, the measured value of 46.0 to 53.5 ºC compared poorly with the model estimate of 350ºC. Estimates made for boiling points ranged from 454 to 848 ºC. The modeled value for TMAC, 848 ºC, compared poorly with the measured value of 121.5 ºC. However, the low boiling point measurement was thought to be the result of impurities; the "true boiling point" was estimated from the experimental work and theoretical properties of the chemical to be > 2000 ºC .

As expected, based on extensive practical experience with these and similar large organic molecules, the EPIWIN estimated vapor pressures were extremely low for the three FND Cationics Category chemicals, and the non-HPV chemicals, DDAC and ADBAC (i.e. nine to 11 orders of magnitude lower than water). A high vapor pressure was reported for the non-HPV chemical, TMAC (1.8 mm Hg). However, this value was considered erroneous and likely due to solvent impurities in the sample. The FND Cationics Category chemicals are essentially nonvolatile, as is generally the case for molecules of this size and complexity.

The EPIWIN estimated values for the octanol/water partition coefficient (log K_{ow}) ranged from 1.22 to 17.9. The value of 4.66 for the non-HPV chemical, DDAC, is compared with the stated log K_{ow} of zero (Appendix B; Ministry of Environment, Lands, and Parks, 1992). The value of 17.9 for the non-HPV chemical, TMAC, suggests that the model cannot adequately calculate values for molecules of such high molecular weight. Attempts to measure the partition coefficient for TMAC did not produce a definitive value with the specified result being > 5.9.

Model predictions for water solubility ranged from insoluble for the non-HPV chemical, TMAC, to slightly soluble (1795 mg/l for CAS RN 112-00-5). The measured value for water solubility of the HPV chemical, CAS RN 61789-80-8, indicated very low solubility of < 0.001 mg/l. The modeled value (0.55 mg/l) for the non-HPV chemical, DDAC, is compared with the published information that the chemical has a water solubility of 700 mg/l (Appendix B; Environment Canada, 1998); this difference in modeled and measured values is consistent with the difference in log K_{ow} noted above. Measurement of water solubility for the non-HPV chemical, TMAC, indicated that the chemical forms a colloidal dispersion in water and the solubility was < 10 mg/l.

Summary - Physical/Chemical Properties

For melting points, model estimates were approximately 3 to 9 times higher than the available measured values. Boiling points were estimated to be high and it is probable that these chemicals would degrade before boiling. Vapor pressures were estimated to be very low (except for the non-HPV chemical, TMAC, where contaminants were thought to confound the measurement), as expected, and the FND Cationics Category chemicals were considered to be essentially nonvolatile. Water solubility estimates varied from insoluble to slightly soluble, with higher solubility predictions tending to occur for lower molecular weight chemicals. Log K_{ow} values less than 5 were predicted for all of the chemicals that could be modeled, except for the non-HPV chemical, TMAC. As noted previously, measurement and prediction of physical/chemical properties for surfactants are complicated by their behavior in test systems and the environment, and the K_{ow} is not an appropriate hydrophobicity parameter for reliably predicting environmental behavior. Although predictions vary, the overall data and knowledge of the chemicals support the conclusion that the FND Cationics Category chemicals have closely related structures and behave similarly from the perspective of physical/chemical properties.

<u>Environmental Fate and Ecotoxicity QSAR Estimates and Correlation to Reliable Data</u>

The available reliable data and QSAR estimates for the environmental fate and effects of the FND Cationics Category chemicals are presented in Table 3. Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

Models for atmospheric photodegradation were used according to EPA guidelines. However, the fugacity models predict virtually no occurrence of the FND Cationics Category chemicals in air. Nonetheless, modeling of the HPV and non-HPV substances indicates that these chemicals would be expected to degrade relatively rapidly upon exposure to light ($t_{1/2}$ values ranging from approximately 2.8 to 5.9 hours). In addition, a measurement for CAS RN 61789-80-8 adsorbed to silica indicated some evidence of photodegradation.

The HYDROWIN model did not provide estimates of stability in water for this class of chemicals because the model cannot calculate this parameter for chemicals that do not meet the criteria of neutral organic compounds with structures that can be hydrolyzed.

An estimation of the transport and distribution of the FND Cationics Category chemicals in environmental media (percent in air, water, soil and sediment) following entry into the environment via water is presented in Table 3. For the HPV and non-HPV chemicals, the model predicts distribution to the water and/or sediment correlated with the predicted water solubility (see above). For chemicals with higher predicted water solubility (CAS RNs 112-00-5 and 112-02-7), the distribution predictions were > 98% to water. For chemicals with lower predicted water solubility (CAS RN 112-03-8, , DDAC, ADBAC, and TMAC), the predictions for water distribution ranged from approximately 5% to 90%, with the remainder primarily in sediment. Some of these estimates may be inaccurate based on the differences in modeled and measured water solubility described above.

For biodegradation, measured data exist for seven of the 13 FND Cationics Category chemicals. In a number of cases, data were available for a two-day, non-standard measurement which indicated very rapid degradation. These tests, measuring disappearance of test substance, are considered of limited value since the high "degradation" is not confirmed in standard tests and presumably the test substance was adsorbed. Other assays indicated degrees of biodegradation varying from none detected to values that would be considered inherently degradable. For the non-HPV chemical, ADBAC, the most recent review by Environment Canada (1998; Appendix B) concludes, “It is not persistent in the water column; movement to the solid phase and microbial degradation are expected to be the main routes of dissipation.” The biodegradation for the non-HPV chemical, TMAC, indicated that no degradation was observed, which was thought most likely to be due to adsorption. In a SCAS test with TMAC, 100% removal was observed in 10 days either via degradation or adsorption. Model predictions for biodegradation were made for the three HPV chemicals in the category with definable structures, as well as for the three non-HPV chemicals. For the two cases for which modeled data could be compared to measured values for HPV chemicals, the model predictions were relatively accurate (e.g. predictions of $t_{1/2}$ values of 15 days for both chemicals with measured degradation rates of approximately 35% in 10 days and of approximately 50% in 28 days). Adsorption phenomena were considered significant confounders in the non-HPV chemical degradation measurements, and thus measured and modeled data could not be compared.

More than 30 studies evaluating the acute and chronic toxicity of the FND Cationics HPV chemicals to aquatic organisms were available. Reliable data for aquatic toxicity of the non-HPV chemicals was also available. In addition, ECOSAR estimates for acute fish and daphnid toxicity were made for the three HPV chemicals with defined structures. The model could not estimate toxicity to algae for these chemicals. Measured acute fish toxicity data were available for five of the 13 FND Cationics Category chemicals and the three non-HPV chemicals. In three of six cases for HPV and non-HPV chemicals, model predictions could be compared to measured values; the model prediction was accurate for CAS RN 112-00-5 (9.77 mg/l for the model and 6.0 mg/l measured), DDAC (2.3 mg/l for the model and a range of approximately 0.3 to 2.8 mg/l measured) and ADBAC (1.78 mg/l for the model and measured values of approximately 0.5 mg/l). The model under-predicted the toxicity for CAS RN 112-02-7 (2.24 mg/l for the model and 0.07 mg/l measured), CAS RN 112-03-8 and TMAC (not toxic at solubility predicted by the model for each chemical, compared to measured values of 0.07 mg/l and approximately 15.1 mg/l, respectively). Measured EC_{50} values for acute toxicity to invertebrates were available for four HPV and the three non-HPV chemicals (values ranging from 0.006 to > 50 mg/l). For CAS RN 68783-78-8, studies for daphnia, Ceriodaphnia, Eastern oyster, mysid shrimp, Pink shrimp and Blue crabs were included in the dataset. Modeled values for acute toxicity to aquatic invertebrates were made for the three FND Cationics Category chemicals and two of the three non-HPV chemicals (TMAC and ADBAC; the model did not provide a value for DDAC). The predicted values were similar to those for fish and none were accurate, with ADBAC modeled value of 1.78 mg/l compared to approximately 0.05 mg/l measured and CAS RN 112-03-8 and TMAC predicted to have no toxicity at solubility with measured values of approximately 0.07 and approximately 15.1 mg/l, respectively. Two FND Cationics Category chemicals (CAS RNs 68783-78-8 (2 studies) and 61789-80-8) had measured EC_{50} values for toxicity to aquatic plants ranging from 0.21 to ≤ 10 and 0.026 to 1.8 mg/l, respectively. A study with TMAC indicated E_bC_{50} (growth; 0-96-hour) of 0.113 mg/l and E_rC_{50} (growth rate; 0-96-hour) of 0.177 mg/l. The Ministry of Environment, Lands, and Parks, (1992; Appendix B) states that the non-HPV chemical, DDAC, is toxic to aquatic plants at approximately 3.5 mg/l.

In addition to the SIDS/HPV endpoints for acute toxicity to aquatic species, chronic toxicity studies with aquatic organisms have been conducted for several FND Cationics Category chemicals. These include studies with fish, Ceriodaphnia, clams, and rotifers for CAS RN 112-00-5 (NOECs and LC_{50} values ranging from approximately 0.05 to >1.25 mg/l), a rotifer study for CAS RN 112-02-7 (LC_{50} value of 0.067 mg/l), a daphnid study for CAS RN 8030-78-2 (NOEC = 6.8 – 99.1 µg/l, and a fish and Ceriodaphnia study for CAS RN 68783-78-8 (NOECs of 12.7 and 0.7 – 0.82 mg/l, respectively). In addition, a toxicity study to bacteria (EC_{50} = 371 mg/l) and chronic toxicity to aquatic invertebrates (NOECs of 0.04, 0.04, and 0.08 mg/l for toxicity, reproduction, and time to first brood, respectively) were available for TMAC. A chronic toxicity to aquatic invertebrates and a fish early life stage assay were also available for ADBAC, with NOECs of 0.00415 and 0.0322 mg/l, respectively.

Summary – Environmental Fate and Ecotoxicity
As anticipated in the EPA guidance for HPV chemicals, only model estimates were available for atmospheric photodegradation and fugacity. The other exclusively modeled value, stability in water, could not be calculated for this category of chemicals. Atmospheric photodegradation was predicted to be rapid, although fugacity models suggested very minimal distribution of these chemicals to the air. Some evidence of photodegradation of one of the FND Cationic Category chemicals was observed when the chemical was bound to silica. Predicted distribution of the chemicals in the environment was to water and/or sediment compartments based on the assumption that release of the chemicals to the environment is exclusively via water. For chemicals with higher predicted water solubility (lower K_{ow}), the water compartment was favored. Measured biodegradation rates were variable and frequently confounded by adsorption. Overall, the FND Cationic Category chemicals are biodegradable, which is consistent with the conclusion of Environment Canada for the non-HPV chemical, DDAC. Measured aquatic toxicity values indicated acute LC_{50} and EC_{50} values generally less than approximately 25 mg/l for fish, daphnid and algae (a single study indicated an LC_{50} > 24 mg/l for fish). Other species may be less sensitive to the toxicity of these surfactants with acute LC_{50} values of 36 and > 50 mg/l recorded for shrimp and crabs, respectively. Chronic toxicity to aquatic organisms varied considerably, with NOECs ranging from 4.15 µg/l to 12.7 mg/l. These studies of aquatic toxicity, many of which were conducted in natural waters with and without added effluents, indicate that the source and composition of the test water dramatically affects the toxicity of the test substance. As noted previously, cationic substances in the environment instantaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments and with dissolved humic substances in surface waters. This complexation behavior results in reduced bioavailability in actual environmental conditions that is not adequately represented by standard laboratory assays and/or predictions by EPIWIN SAR models. Thus the extreme variability of the measured values is predictable. Further, as would be anticipated, the modeling programs were inconsistent in their accuracy for aquatic toxicity endpoints with some values similar to measured or expected and others divergent. Overall, the available data support the conclusion that, because of their closely-related structures, FND Cationics Category chemicals possess similar environmental fate and ecotoxicity across the category.

Human Health-Related Reliable Data

The human health effects data for SIDS endpoints of the 13 FND Cationics Category chemicals and three related supplemental chemicals are presented in Table 4. Robust summaries for the reliable studies, including studies on the non-HPV chemical, TMAC, are provided in

Appendix A. References for reliable studies on the non-HPV chemicals, ADBAC and DDAC, are provided in Appendix B.

Rat acute oral toxicity LD_{50} data were available for nine of the 13 FND Cationics Category chemicals and two of the non-HPV chemicals, TMAC and DDAC. For the FND Cationics Category chemicals, rat oral LD_{50}s range from approximately 200 to > 2000 mg/kg indicating that the chemicals possess moderate to slight acute toxicity by the oral route. Stated LD_{50} values for DDAC ranged from approximately 60 to 400 mg/kg and a value > 16,300 mg/kg was determined for TMAC. Rabbit acute dermal toxicity studies for two FND Cationics Category chemicals (CAS RN 112-02-7 and 8030-78-2) failed to confirm an LD_{50} but suggest that the value is slightly less than 4000 mg/kg indicating these chemicals have minimal acute toxicity in rabbits via skin application. Percutaneous LD_{50}s for DDAC ranged from > 228 to > 3480 mg/kg, and a percutaneous LD_{50} > 2000 mg/kg was determined for TMAC. In addition, an acute inhalation study for the FND Cationics Category chemical, CAS RN 61789-80-8, indicted this chemical caused no toxicity at > 180 mg/l following a 1-hour exposure. Additional information (included as Additional Remarks in Robust Summaries Appendix A) indicated very little skin penetration (≈ 0.5% of the dose) of CAS RN 68391-05-9 following a single application of radiolabeled chemical.

A repeated dose toxicity study was available for four of the FND Cationics Category chemicals (CAS RNs 112-02-7, 68391-05-9, 61789-80-8 and 61789-81-9). Repeated dermal dose studies in rabbits for CAS RNs 112-02-7 (28-day) and 68391-05-9 (13-weeks) were conducted using a single dose of 10 mg/kg/day since this was the highest dose that could be applied based on irritation. No effects except for mild irritation were observed. For CAS RN 61789-80-8, a 90-day toxicity study in dogs was reported with a NOAEL > 100 mg/kg/day, the highest dose tested. There were no effects related to toxicity of the test substance in this study. Skin irritation but no other toxic effects were observed following 13 weeks of dermal dosing in rabbits with 10 or 140 mg/kg/day. Additional information (included as Additional Remarks in Robust Summaries Appendix A) indicated that following 90 days of dosing 2800 ppm of this chemical in the diet of rats, approximately 16% of the consumed dose was found in the excreta of males and 6% in excreta of females. In a rat subchronic study of 13 or 22 weeks duration, no NOAEL was established for CAS RN 61789-81-9. The LOAEL was reported to be 170 mg/kg/day. The treatment-associated changes observed were principally in the mesenteric and pulmonary lymph nodes, adrenal glands and liver. A number of subchronic and chronic toxicity studies were available for the three non-HPV chemicals (DDAC, TMAC and ADBAC). At high doses (approximately 500 mg/kg/day and greater) DDAC and ADBAC are lethal to rats due to localized effects in the gastrointestinal tract. At doses below those that result in severe, direct effects on the g.i. tract, these studies indicate no organ-specific toxicity, with effects in 90-day and chronic toxicity studies limited to body weight changes and other general responses. NOAELs for the studies with DDAC ranged from 10 mg/kg/day in a chronic dog study to > 100 mg/kg/day in 90-day rat studies. The NOAELs for studies with ADBAC were > 20 mg/kg/day for a dermal 90-day study in rats (dose levels limited by irritant properties of the test substance) and approximately 40 mg/kg/day for an oral 90-day study in rats. The NOAEL for ADBAC was approximately 80 mg/kg/day for chronic toxicity studies in rats and mice. A subchronic study with TMAC reported a NOAEL of 40 mg/kg/day with histiocytic hyperplasia of the mesenteric lymph nodes being the only finding of significance at 200 and 1000 mg/kg/day.

In vitro genetic toxicity studies (*Salmonella* reverse mutation assay) for five of the FND Cationics Category chemicals were identified. CAS RN 112-00-5 was negative in a standard assay. Three tests for two of the chemicals (CAS RNs 112-02-7 and 112-03-8) indicated no mutagenic activity, but only two tester strains were evaluated. Inconsistent results were observed for CAS RN 8030-78-2 with one test indicating no mutagenic activity and a second showing a minimal, three-fold, increase in back mutations in one of the cell lines tested. A test with CAS RN 61789-77-3 was negative in the four tester strains used. CAS RN 112-00-5 was also negative in the *in vitro* mouse lymphoma and UDS assays as well as in an *in vivo* cytogenetics assay. A nonstandard *in vitro* test examining morphological transformations for CAS RN 112-02-7 was also negative and an *in vivo* mouse micronucleus assay for CAS RN 68783-78-8 was negative. Results from a series of *in vitro* tests were available for the two non-HPV chemicals, DDAC and ADBAC. There were no mutagenic effects, no effect on DNA synthesis, and no chromosomal aberrations observed. In addition, a *Salmonella* reverse mutation assay and an *in vivo* mammalian bone marrow cytogenetics assay were negative for the non-HPV chemical, TMAC. Overall, the available data indicate the chemicals in the FND Cationics Category are unlikely to be mutagenic, as would be expected based on the structures, molecular weights, and knowledge of related chemicals.

For the FND Cationics Category chemicals, evaluation of potential reproductive effects is satisfied by the histological evaluation of reproductive organs in the repeat dose toxicity study in dogs for CAS RN 61789-80-8 and in rats for CAS RN 61789-81-9. No effects on the gonads or other reproductive organs were observed at any dose level in these studies. Thus the NOAELs for reproductive screening were > 100 mg/kg/day for CAS RN 61789-80-8 and > 750 mg/kg/day for CAS RN 61789-81-9. Two-generation reproduction studies in rats were available for the two non-HPV chemicals, DDAC and ADBAC. The NOAEL for DDAC was approximately 56 mg/kg/day for adult and offspring toxicity, with no reproductive effects found. For ADBAC, the NOAELs for toxicity were > 146 mg/kg/day for parents and 73 mg/kg/day for offspring, with no reproductive effects noted.

Developmental toxicity studies were available for five FND Cationics Category chemicals (CAS RNs 112-00-5, 112-02-7, 112-03-8, 68783-78-8 and 61789-81-9) and the two non-HPV chemicals, DDAC and ADBAC. For CAS RN 112-00-5, the oral NOAEL for maternal and developmental toxicity was 24 mg/kg/day with no embryo/fetal toxicity or teratogenicity observed. For CAS RNs 112-02-7, the percutaneous NOAEL for maternal and developmental toxicity in rabbits was > 10 mg/kg/day and for CAS RN 112-03-8, the percutaneous NOAELs for maternal and developmental toxicity in rats were > 12.5 mg/kg/day. No embryo/fetal toxicity or teratogenicity was observed in either study. Studies for CAS RNs 68783-78-8 and 61789-81-9 with two dose levels (100 and 500 mg/kg/day) via gavage and a single dietary concentration (to yield a target dose of 500 mg/kg/day) were available. The NOAEL for maternal toxicity for CAS RN 68783-78-8 was > 500 mg/kg/day via gavage but no NOAEL was established via diet, with minimal body weight and feed consumption changes noted. The developmental NOAEL for this chemical was > 500 mg/kg/day by either exposure route. For CAS RN 61789-81-9, the maternal and developmental NOAELs were greater than the highest dose by either route of exposure (500 or 475 mg/kg/day via gavage or diet, respectively). Results for two developmental toxicity studies were available for the non-HPV chemical, DDAC. The NOAELs for rabbits were 1.0 and 3.0 mg/kg/day for maternal and developmental toxicity, respectively.

Corresponding values for rats were 1.0 and 20.0 mg/kg/day. No teratogenic effects were observed for either species. For the non-HPV chemical, ADBAC, the oral maternal and developmental NOAELs were 10 and > 100 mg/kg/day, respectively for rats, and 3 and > 9 mg/kg/day for rabbits with no embryo/fetal toxicity or teratogenicity observed.

Summary – Human Health-Related Data

Adequate acute oral LD_{50} studies were available throughout the category. They indicate minimal to moderate acute toxicity of the chemical class with LD_{50} values ranging from approximately 60 to > 16,000 mg/kg. Repeat dose toxicity studies supported the conclusion that the chemicals in the FND Cationics Category have minimal toxicity potential below acutely toxic doses. Available *in vitro* and *in vivo* assays indicated the FND Cationics Category chemicals and supplemental chemicals are unlikely to have mutagenic activity. A reproductive screening evaluation from two repeat dose toxicity studies, two reproductive toxicity studies and results from available developmental toxicity studies, indicated that the FND Cationics Category chemicals are unlikely to cause reproductive effects and are not developmental toxicants. The available data support the conclusion that, because of their closely-related structures and similar physical/chemical properties, the FND Cationics Category chemicals possess similar human health-related effects across the category.

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Table 1. Structures of FND Cationics Category Chemicals

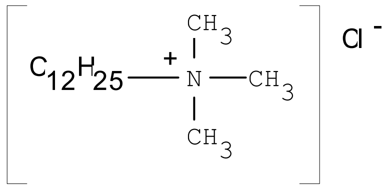
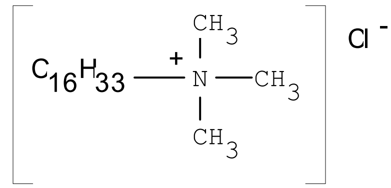
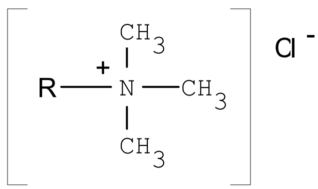
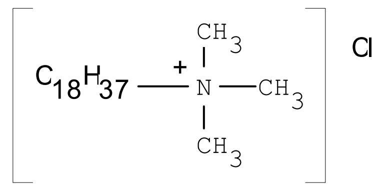
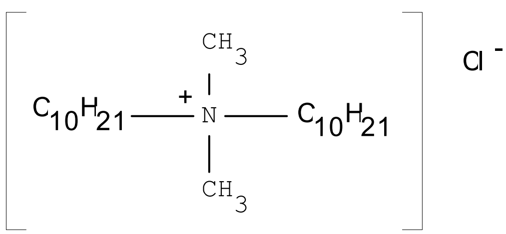
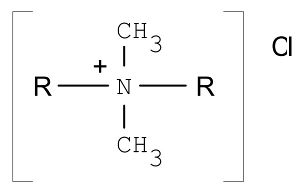
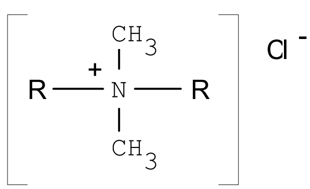
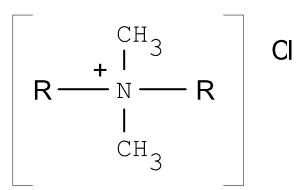
 Ammonium, dodecyltrimethyl-, chloride 112-00-5	 Ammonium, hexadecyltrimethyl-, chloride 112-02-7
 **R = tallow alkyl** Quaternary ammonium compounds, trimethyltallow alkyl, chlorides 8030-78-2	 Trimethyloctadecylammonium chloride 112-03-8
 *non-HPV* *Didecyldimethylammonium chloride (DDAC)* *7173-51-5*	 **R = coco alkyl** Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides 61789-77-3
 **R = $C_{12} – C_{18}$ alkyl** Quaternary ammonium compounds,di-C_{12-18}-alkyldimethyl, chlorides 68391-05-9	 **R = $C_{14} – C_{18}$ alkyl** Quaternary ammonium compounds, di-C_{14-18}-alkyldimethyl, chlorides 68002-59-5

Table 1. Structures of FND Cationics Category Chemicals (continued)

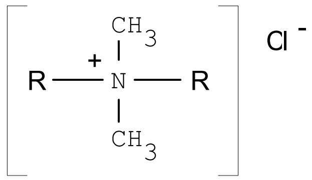
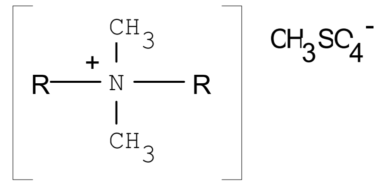
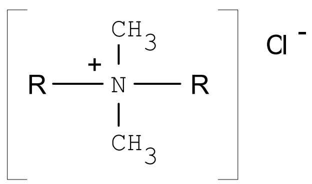
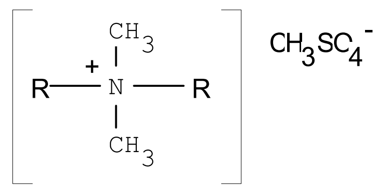
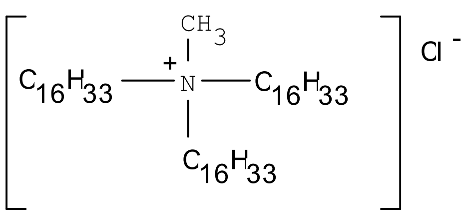
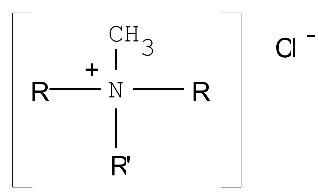
 **R = tallow alkyl** Quaternary ammonium compounds, dimethylditallow alkyl, chlorides 68783-78-8	 **R = C_{14} – C_{18} alkyl** Quaternary ammonium compounds, di-$C_{14–18}$-alkyldimethyl, Me sulfates 68002-58-4
 **R = hydrogenated tallow alkyl** Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride 61789-80-8	 **R = hydrogenated tallow alkyl** Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, Me sulfates 61789-81-9
 *non-HPV* *1-Hexadecanaminium, N, N-dihexadecyl-N-methyl-, chloride* *(Tricetylmethylammonium chloride, TMAC)* *52467-63-7*	 **R = hydroxyethyl** **R' = tallow alkyl** Quaternary ammonium compounds, bis(hydroxyethyl)methyltallow alkyl, chlorides 67784-77-4

Table 1. Structures of FND Cationics Category Chemicals (continued)

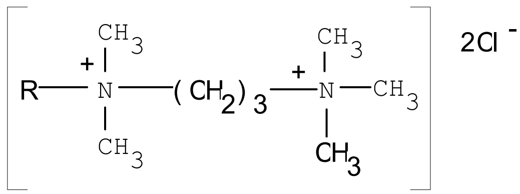
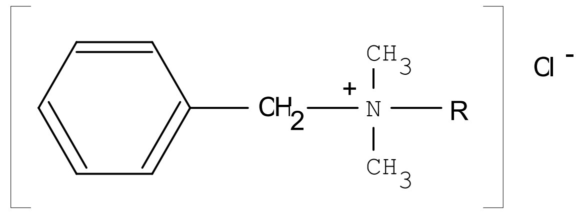
	
R = tallow alkyl	**R = $C_{12} – C_{16}$ alkyl**
Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichloride 68607-29-4	*non-HPV* *Alkyl (C_{12-16}) dimethylbenzylammonium chloride (ADBAC) 68424-85-1*

Table 2. Physical/Chemical Properties Data for FND Cationics Category Chemicals (continued)

CAS RN	**Melting Point (ºC)**	**Boiling Point (ºC)**	**Vapor Pressure (mm Hg)**	**Partition Coefficient (log K_{ow})**	**Water Solubility (mg/l)**
112-00-5	182	454	9.3 E-9	1.22	1795
112-02-7	213	500	2.8 E-10	3.23	16.3
8030-78-2					
112-03-8	223	523	5.4 E-11	4.17	1.76
7173-51-5 non-HPV	*229*	*535*	*2.3 E-11*	*4.66* ***0***	*0.55* ***700***
61789-77-3					
68391-05-9					
68002-59-5					
68783-78-8					
68002-58-4					
61789-80-8	**50 - 60**				**< 0.001**
61789-81-9					
52467-63-7 non-HPV	*350* ***46.0 – 53.5***	*848* ***121.5*** [a]	*3 E-21* ***1.8*** [b]	*17.9* ***> 5.9*** [c]	*Insoluble* ***< 10 mg/l forms a colloidal dispersion***
67784-77-4					
68607-29-4					
68424-85-1 non-HPV	*241*	*561*	*3.5 E-12*	*3.91*	*2.2*

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.
Regular font indicates data obtained from appropriate models as described in the text.
CAS RN and data in italics are for supplemental chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.

[a] The "true boiling point" was calculated to be > 2000 ºC; the measured value was considered to be affected by impurities.

[b] Calculated value at 25 ºC using the measured boiling point; the value is considered inaccurate based on the structure of the chemical, and the high vapor pressure is considered likely to be associated with solvent impurities.

[c] Estimated according to Guideline OECD 107 (see Robust Summary).

Table 3. Environmental Fate and Ecotoxicity Data for FND Cationics Category Chemicals

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution	Biodegradation	Acute Tox. to Fish LC_{50} (mg/l)	Acute Tox. to Invertebrates EC_{50} (mg/l)	Toxicity to Aquatic Plants EC_{50} (mg/l)	Chronic Toxicity to Aquatic Species (mg/l)[a]
112-00-5	k_{phot} = 28.5 E-12 $t_{1/2}$ = 4.5 hr	NC	air: < 1% water: 99.8% soil: < 1% sediment: < 1%	$t_{1/2}$ water = 15 d $t_{1/2}$ soil = 15 d $t_{1/2}$ sediment = 60 d **35% by 10 d** **98% by 2 d**	9.77 **6.0**	3.24 **0.39** **0.345**	NBD	**NOEC Fish = 0.5 to > 1.25** **LC_{50} CD = 0.31** **LC_{50} CD = 0.30 – 0.45** **NOEC CD = 0.05 – 0.25** **NOEC CD (Surv.) = 0.25** **NOEC Clam ≈ 0.046 (8 wk)** **EC_{50} Rotifer = 0.23 (48 h)**
112-02-7	k_{phot} = 34 E-12 $t_{1/2}$ = 3.9 hr	NC	air: < 1% water: 98.5% soil: < 1% sediment: < 1.5%	$t_{1/2}$ water = 15 d $t_{1/2}$ soil = 15 d $t_{1/2}$ sediment = 60 d **82% by 2 d** **65% BOD/ThOD by 28 d (75% by 42 d)** **48% BOD/ThOD by 28 d (60% by 56 d)**	2.24 **0.07**	1.59	NBD	**EC_{50} Rotifer = 0.067 (48 h)**
8030-78-2				**95% by 2 d** **48% BOD/ThOD by 28 d (51% by 35 d)** **53% BOD/ThOD by 28 d (79% by 56 d)** **40% BOD/COD by 28 d (61% by 42 d)**		**0.0126 – 0.0989**		**NOEC Daphnia = 0.0068 – 0.0991 (21 d)**
112-03-8	k_{phot} = 37 E-12 $t_{1/2}$ = 3.5 hr	NC	air: < 1% water: 83.3% soil: < 1% sediment: 16.7%	$t_{1/2}$ water = 37.5 d $t_{1/2}$ soil = 37.5 d $t_{1/2}$ sediment = 150 d **98% by 2 d**	Not toxic at solubility **0.07**	Not toxic at solubility	NBD	
7173-51-5 non-HPV	*k_{phot} = 46.3 E-12* *$t_{1/2}$ = 5.5 hr*	*NC* ***Stable (pHs 5, 7, 9 for 30 d)***	*air: < 1%* *water: 78.9%* *soil: < 1%* *sediment: 21.1%* ***Immobile in soil***	*$t_{1/2}$ water = 15 d* *$t_{1/2}$ soil = 15 d* *$t_{1/2}$ sediment = 60 d* ***Degradable***	*2.3* ***0.3 – 2.4 (48 hr)*** ***0.27 –2.8 (96 hr)***	***0.09 (daphnia)*** ***0.07 (mysid)***	***≈ 3.5***	

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.
Regular font indicates data obtained from appropriate models as described in the text.
CAS RN and data in italics are for supplemental chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.
NC = Not calculable for FND Cationic Category chemicals with the HYDROWIN submodel.
NBD = ECOSAR model has not been developed to predict algal toxicity for cationic surfactants.

[a] Values are for 7-day studies unless indicated otherwise; CD = Ceriodaphnia; Surv. = Survival (value for reproduction also available – see Robust Summary);

Table 3. Environmental Fate and Ecotoxicity Data for FND Cationics Category Chemicals (continued)

CAS RN	Photodegradation (cm^3/molecule-sec for k_{phot})	Stability in Water	Transport & Distribution	Biodegradation	Acute Tox. to Fish LC_{50} (mg/l)	Acute Tox. to Invertebrates EC_{50} (mg/l)[a]	Toxicity to Aquatic Plants EC_{50} (mg/l)	Chronic Tox. to Aquatic Species (mg/l)[b]
61789-77-3				**0% BOD/ThOD by 28 d (56% by 214 d)** **80.3% by 2 d**				
68391-05-9								
68002-59-5								
68783-78-8					**0.62 to > 24.0** **24**	**CD = 0.54 – 1.23** **DM = 0.19 – 1.06** **Oyster = 2.0** **MS = 0.22 (96 h)** **Shrimp = 36** **Crab > 50**	**1.12** **0.21 to ≤ 10[c]**	**NOEC Fish = 12.7** **LC_{50} CD = 0.70** **LC_{50} CD = 0.82**
68002-58-4								
61789-80-8	**Evidence of photodegradation when absorbed to silica**			**35% BOD by 20 d** **4.8% ThOD by 26 d** **79% by 2 d**	**1.33** **4.22** **3.4** **0.29 – 14**	**0.065 – 3.6**	**0.026 – 1.8**	
61789-81-9								
52467-63-7 non-HPV	*k_{phot} = 92.4 E-12* *$t_{1/2}$ = 2.8 hr*	*NC*	*air: < 0. 1%* *water: 4.8%* *soil: < 0.1%* *sediment: 95.2%*	*$t_{1/2}$ water = 37.5 d* *$t_{1/2}$ soil = 37.5 d* *$t_{1/2}$ sediment = 150 d* ***No degradation observed*** ***100% removal in 12 days - adsorption likely***	*Not toxic at solubility* ***≈15.1***	*Not toxic at solubility* ***0.11***	*NBD* **E_bC_{50} (0-96-hour) = 0.113;** **E_rC_{50} (0-96-hour) = 0.177**	***NOEC DM (Toxicity) = 0.04;*** ***NOEC (Repro.) = 0.04;*** ***NOEC (Time to First Brood) = 0.08*** ***Toxicity to Bacteria;*** ***EC_{50} = 371***
67784-77-4								
68607-29-4				**12% BOD/ThOD by 182 d**				
68424-85-1 non-HPV	*k_{phot} =4.36 E-11* *$t_{1/2}$ = 5.9 hr*	*NC*	*air: < 0.1%* *water: 4.7%* *soil: 94.7%* *sediment: 0.5%*	*$t_{1/2}$ water = 37.5 d* *$t_{1/2}$ soil = 37.5 d* *$t_{1/2}$ sediment = 150 d*	*1.78* ***0.515*** ***0.923*** ***0.28*** ***0.86***	*1.78* ***0.0058*** ***0.055*** ***0.092***	*NBD*	***Fish early life stage: NOEC = 0.0322;*** ***NOEC DM = 0.00415***

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.
Regular font indicates data obtained from appropriate models as described in the text.
CAS RN and data in italics are for supplemental chemicals [non-HPV].
Empty block denotes data either are not available or are available and judged inadequate.
NC = Not calculable for FND Cationics Category chemicals with the HYDROWIN submodel.
NBD = ECOSAR model has not been developed to predict algal toxicity for cationic surfactants.

[a] All values are for 48-hours unless specified; CD = Ceriodaphnia; DM = Daphnia magna; MS = Mysid shrimp
[b] Values are for 7-day studies unless indicated otherwise; CD = Ceriodaphnia; DM = Daphnia magna; Repro. = Reproduction
[c] Values are algaestatic concentrations for several species

Table 4. Human Health-Related Data for FND Cationics Category Chemicals

CAS RN	Acute Oral Toxicity LD_{50} (mg/kg)	Acute Inhalation Toxicity LC_{50} (mg/l)	Acute Dermal Toxicity LD_{50} (mg/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
112-00-5	**490** **560**				**Negative (Ames)** **Negative (mouse lymphoma)** **Negative (UDS in vitro)** **Negative (*In vivo* cytogenetic)**		**Maternal = 24** **Developmental = 24**[a]
112-02-7	**400 < LD_{50} < 600**		**≈ 4300** [b]	**10**[c]	**Negative (Ames)** [d] **Negative (Ames)** [d] **Did not produce morphological transformations**		**Maternal > 10** **Developmental > 10**[e]
8030-78-2	**1260**		**< 4000** [f] **< 4700**		**Negative (Ames)** **Positive (Ames)** [g]		
112-03-8	**633 (M)** **536 (F)**				**Negative (Ames)** [d]		**Maternal > 12.5** [h] **Developmental > 12.5**

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.
Regular font indicates data obtained from appropriate models as described in the text.
Empty block denotes data either are not available or are available and judged inadequate.
M = male
F = female

[a] Oral study in rabbits.
[b] 50% mortality at the only dose tested.
[c] 28-Day dermal toxicity study in rabbits; the NOAEL is for systemic toxicity with skin irritation observed at the 10 mg/kg/day dose.
[d] Only two tester strains used in *Salmonella* reverse mutation assay.
[e] Dermal application in rabbits; skin irritation at all doses in dams; no embryo/fetal toxicity or teratogenicity observed.
[f] More than 50% mortality at the only dose tested.
[g] Three-fold increase in back mutations in a single cell line (TA 1538).
[h] Dermal application in rats (no embryo/fetal toxicity or teratogenicity observed).

Table 4. Human Health-Related Data for FND Cationics Category Chemicals (continued)

CAS RN	Acute Oral Toxicity LD_{50} (mg/kg)	Acute Inhalation Toxicity LC_{50} (mg/l)	Acute Dermal Toxicity LD_{50} (mg/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
7173-51-5 non-HPV	***59.5 - 399***		***> 228 - 3480***	***> 12 [i] 107 [j] 61 [j] 10 [k] 32 [l] 76 [m]***	***Not mutagenic No chromosomal aberrations No effect on DNA synthesis***	***Parental and offspring ≈ 56 No reproductive effects***	***Rabbit maternal = 1.0 Developmental = 3.0 Rat maternal = 1.0 Developmental = 20.0***
61789-77-3	**960**				**Negative (Ames) [n]**		
68391-05-9	**4700**			**100 [o]**			
68002-59-5							

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.
CAS RN and data in italics are for supplemental chemicals [non-HPV].
Regular font indicates data obtained from appropriate models as described in the text.
Empty block denotes data either are not available or are available and judged inadequate.

[i] 13-week dermal toxicity study in rats.
[j] 90-day feeding toxicity study in rats.
[k] 52-week oral toxicity study in dogs.
[l] Chronic toxicity study in rats.
[m] Chronic toxicity study in mice.
[n] TA 98, TA 100, TA 1535 and TA 1537 were tested.
[o] 28/91-day dermal toxicity study in rabbits; the NOAEL is for systemic toxicity with skin irritation observed in the treated animals at 100 mg/kg/day.

Table 4. Human Health-Related Data for FND Cationics Category Chemicals (continued)

CAS RN	Acute Oral Toxicity LD_{50} (mg/kg)	Acute Inhalation Toxicity LC_{50} (mg/l)	Acute Dermal Toxicity LD_{50} (mg/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
68783-78-8	**> 2150**				**Negative (*In vivo* mouse micronucleus)**		**Maternal > 500 via gavage Developmental > 500 via gavage or diet [p]**
68002-58-4							
61789-80-8	**> 500 > 576 [q] > 432 [q]**	**> 180 (1 hr)**		**> 100 [r] 140 [s]**		**> 100 [t]**	
61789-81-9				**LOAEL ≈ 170 [u]**		**> 750 [v]**	**Maternal > 500 via gavage; > 475 via diet Developmental > 500 via gavage; > 475 via diet [p]**

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.
Regular font indicates data obtained from appropriate models as described in the text.
Empty block denotes data either are not available or are available and judged inadequate.

[p] Developmental toxicity study conducted in rats at two gavage doses (100 or 500 mg/kg/day) or a single dietary concentration to provide a target dose of 500 mg/kg/day).
[q] Toxicity study conducted with mice (LD_{50} > 576) and dogs (LD_{50} > 432).
[r] 90-day oral toxicity feeding study in dogs.
[s] 91-day dermal toxicity study in rabbits; the NOAEL is for systemic toxicity with skin irritation observed at both the 10 and 140 mg/kg/day doses.
[t] Evaluation of reproductive organs from the 90-day oral feeding study in dogs adequate for SIDS reproductive screening (included in Robust Summary for 90-day study).
[u] 13-Week feeding toxicity study in rats extended to 22 weeks for satellite group; NOAEL was not established at either time point.
[v] Evaluation of reproductive organs from the 13/22-week oral feeding study in rats adequate for SIDS reproductive screening (included in Robust Summary for 13/22-week study).

Table 4. Human Health-Related Data for FND Cationics Category Chemicals (continued)

CAS RN	Acute Oral Toxicity LD_{50} (mg/kg)	Acute Inhalation Toxicity LC_{50} (mg/l)	Acute Dermal Toxicity LD_{50} (mg/kg)	Repeated Dose Toxicity NOAEL (mg/kg/day)	Genetic Toxicity	Toxicity to Reproduction NOAEL (mg/kg/day)	Developmental Toxicity NOAEL (mg/kg/day)
52467-63-7 non-HPV	***> 16,300***		***> 2000***	***40***	***Negative (Ames) Negative (In vivo cytogenetic)***		
67784-77-4							
68607-29-4	**205**						
68424-85-1 non-HPV				***> 20 [w] ≈ 40 [g] ≈ 80 [x] ≈ 83 [y]***	***Not mutagenic No chromosomal aberrations No effect on DNA synthesis***	***Parental > 146 Offspring = 73 Reproduction > 146***	***Maternal = 10 Developmental > 100 [z] Maternal = 3 Developmental > 9 [aa]***

Note: Bold font indicates reliable data for which Robust Summaries are provided in Appendix A, or are included in references for reliable studies on the non-HPV chemicals, DDAC (CAS RN 7173-51-5) and ADBAC (CAS RN 68424-85-1), provided in Appendix B.
CAS RN and data in italics are for supplemental chemicals [non-HPV].
Regular font indicates data obtained from appropriate models as described in the text.
Empty block denotes data either are not available or are available and judged inadequate.

[g] 90-day feeding toxicity study in rats.
[w] 90-day dermal toxicity study in rats.
[x] Combined chronic toxicity/oncogenicity study in rats (NOAEL is for toxicity; no evidence of carcinogenicity).
[y] Combined chronic toxicity/oncogenicity study in mice (NOAEL is for toxicity; no evidence of carcinogenicity).
[z] Developmental toxicity study in rats via gavage.
[aa] Developmental toxicity study in rabbits via gavage.

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Appendix A

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Appendix A

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5.4 REPEATED DOSE TOXICITY

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5.5 GENETIC TOXICITY *IN VITRO*

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5.10 ADDITIONAL REMARKS

2.1 Melting Point

Test Substance

Identity:	Dihydrogenatedtallow dimethyl ammonium chloride (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)
Purity:	75 - 78% (commercial grade) 100% (pure form)
Remarks:	

Method

Method/Guideline followed:	Not stated
GLP:	Not stated
Year:	Not stated
Remarks:	

Results

Melting Point:	30 - 45°C (commercial grade) 50 - 60°C (pure form)
Decomposition:	Decomposition occurs at approximately 135°C
Sublimation:	Not stated
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions, data provided in a reliable source.

References

European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). 1993. DHTDMAC: Aquatic and Terrestrial Hazard Assessment. CAS RN 61789-80-8. Technical Report number 53, ISSN-0773-8072-53. ECETOC, Brussels, Belgium.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	20c
Remarks:	

2.1 MELTING POINT

Test Substance

Identity:	ARQUAD 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	70.4%
Remarks:	

Method

Method/Guideline followed:	OECD Guideline No. 102, EEC Method A1
GLP:	Yes
Year:	1990
Remarks:	Determination was carried out by a capillary tube method using a Buchi 530 melting/boiling point apparatus to provide the heating.

Results

Melting point value:	46.0 to 53.5 °C (319 to 326.5 K) mean of 45.5 – 53.5 °C and 46.5 – 53.5 °C
Decomposition:	No
Sublimation:	No
Remarks:	A melting point determination on a sample of “dried” test substance also was performed. The melting range was 65.5 to 70.5 °C (338.5 to 343.5 K). This increase in melting range probably reflects the increase in “purity” of the test substance.

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; guideline study (OECD, ECC).

References

O’Connor, J. 1990. Arquad 3.16: Determination of Physico-chemical Properties. Report number 90/AKL013/0587. Akzo Chemicals International, BV, The Netherlands.

Other

Last changed:	May 14, 2001
Order number for sorting:	30
Remarks:	

2.2 BOILING POINT

Test Substance

Identity:	ARQUAD 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	70.4%
Remarks:	

Method

Method/Guideline followed:	OECD Guideline No. 103, EEC Method A2
GLP:	Yes
Year:	1990
Remarks:	Determination was carried out by a modified Siwoloboff method using a boiling point tube and capillary in a Buchi 530 melting/boiling point apparatus. It was possible to estimate the true boiling point based on the structure of ARQUAD 3.16. The method described by Meissner is based on the correlation of the normal boiling point with chemical type; molar refraction, $[R_D]$, and parachor, [P], are used as variables in the correlation: $T_b = (637\ [R_D]^{1.47} + B)/[P]$ where B is a constant whose value depends upon the chemical type.

Results

Boiling point value:	121 and 122 °C (394 and 395 K); mean value = 121.5 °C (394.5 K)
Pressure:	Not stated
Pressure unit:	Not stated
Decomposition:	Described below
Remarks:	A boiling point determination on a sample of "dried" test substance also was performed. When the test substance was heated above 106 °C the liquid became opaque and darkened in color, becoming a brown liquid. The boiling point was determined to be 167 °C, but signs of decomposition occurred above 106 °C. The estimated boiling point $[T_b]$ was calculated to be 2834 K (2561 °C) using McGowan's [P] value, or 2824 K (2551 °C) using Sugden's [P] value.

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; guideline study (OECD, ECC).

References

O'Connor, J. 1990. Arquad 3.16: Determination of Physico-Chemical Properties. Report number 90/AKL013/0587. Akzo Chemicals International, BV, The Netherlands.

Other

Last changed:	May 14, 2001
Order number for sorting:	30
Remarks:	

2.4 Vapor Pressure

Test Substance

Identity:	ARQUAD 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	70.4%
Remarks:	

Method

Method/Guideline followed:	OECD Guideline No. 104, EEC Method A4
GLP:	Yes
Year:	1990
Remarks:	Because the test substance contained 7.6% water, a "dry" sample of the test substance was prepared prior to testing. Then, using the apparent boiling point of the dried test substance (167 °C) the vapor pressure was extrapolated using a rearrangement of the equation of Hass and Newton for the correction of boiling point to standard pressure:

$$2.8808-\log_{10}P = (\phi \times \Delta t)/((273.1 + t) - (0.15 \times \Delta t))$$

where:

- Δt = ºC to be added to the observed boiling pt.
- t = observed boiling pt.
- $\log_{10}P$ = the logarithm of the observed pressure (mm Hg)
- ϕ = the entropy of vaporization at 760 mm Hg

Results

Vapor pressure value:	174 and 245 Pa (1.3 and 1.8 mmHg) at 20 and 25 ºC, respectively (estimated)
Temperature °C:	Described above
Decomposition:	Described below
Remarks:	It is not certain that this value reflects the true vapor pressure. It appears to be too high when one considers the nature of the test substance (it is possible that the test substance could contain traces of water and/or isopropanol). Alternatively, one can surmise from the estimated boiling point, > 2000 ºC, that the true vapor pressure of the tests substance is so low as to be not measurable, and that it will decompose on heating. (Author)

Conclusions

Remarks: The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; guideline study (OECD, ECC).

References

O'Connor, J. 1990. Arquad 3.16: Determination of Physico-Chemical Properties. Report number 90/AKL013/0587. Akzo Chemicals International, BV, The Netherlands.

Other

Last changed: May 14, 2001

Order number for sorting: 30

Remarks:

2.5 Partition Coefficient

Test Substance

Identity:	ARQUAD 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	70.4%
Remarks:	

Method

Method/Guideline followed:	OECD Guideline No. 107, EEC Method A8
GLP:	Yes
Year:	1990
Remarks:	The value of Log K_{ow} for the test substance was calculated by the Leo and Hansch procedure. The partition coefficients can be determined preferably for pure, non-surface active, water-soluble substances that do not associate or dissociate in solution. This test substance is a surface-active substance; therefore, the accurate experimental determination of the partition coefficient (n-octanol/water) is not possible. However, an estimate of the partition coefficient is made by measuring the solubility of the test substance in n-octanol and water. It was not possible to determine the water solubility of ARQUAD 3.16 due to the nature of the test substance; but it was reported to be less than 10 mg/l.

Results

Log K_{ow}:	> 5.86 (estimated)
Temperature ºC:	20 ºC
Remarks:	None

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; guideline study (OECD, ECC).

References O'Connor, J. 1990. Arquad 3.16: Determination of Physico-Chemical Properties. Report number 90/AKL013/0587. Akzo Chemicals International, BV, The Netherlands.

Other

Last changed: May 14, 2001
Order number for sorting: 30
Remarks:

2.6 Water Solubility

Test Substance

Identity: Dihydrogenatedtallow dimethyl ammonium chloride (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)

Purity: 100% (pure form)
75 – 78% (commercial grade)

Remarks:

Method

Method/Guideline followed: Not stated

GLP: Not stated

Year: Not stated

Remarks:

Results

Value: < 1 µg/l

Solubility: < 1 µg/l (pure form and commercial grade)

pH value and concentration: Not stated

pKa value at 25°C: Not stated

Remarks:

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability: 2D

Remarks: Reliable with restrictions; information provided in an ECETOC technical report.

References

European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). 1993. DHTDMAC: Aquatic and Terrestrial Hazard Assessment. CAS RN 61789-80-8. Technical Report number 53, ISSN-0773-8072-53. ECETOC, Brussels, Belgium.

Other Available Reports

Other

Last Changed: December 13, 2001

Order number for Sorting: 20c

Remarks:

2.6 WATER SOLUBILITY

Test Substance

Identity:	ARQUAD 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	70.4%
Remarks:	

Method

Method/Guideline followed:	OECD Guideline No. 105, EEC Method A6
GLP:	Yes
Year:	1990
Remarks:	Because the aqueous solubility of the test substance was reported to be less than 10 mg/l, the solubility was attempted by the column elution method. Water was circulated through the system from approximately 16 hours, at which time the circulating water was hazy. Non-dissolved test substance was observed as a colloidal suspension and this test method was terminated. A preliminary flask shaking test was performed by adding 200 ml of distilled water to 0.2, 2 and 20 g of ARQUAD 3.16 (nominal concentrations = 1, 10 and 100 g/l, respectively). The samples were shaken in a water bath at 20 °C for two days. The samples were transferred to centrifuge tubes and centrifuged (260 rpm for 90 minutes) in an attempt to produce a clear, saturated supernatant.

Results

Value at 20 °C:	The test substance appeared to be infinitely miscible as a colloidal dispersion with water.
Description of solubility:	Described above
pH value/concentration 20 °C:	Not stated
pKa value at 25 °C	Not stated
Remarks:	In all samples of the flask shaking test with subsequent centrifugation, there was an observable gradation of test substance from bottom to the top of the centrifuge tube, but not a clear supernatant, and as the ratio of test substance to distilled water increased, the samples appeared more hazy. This is because the relative density of ARQUAD 3.16 is 0.93 and it forms a colloidal suspension in water.

Conclusions

Remarks: The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; guideline study (OECD, ECC).

References

O'Connor, J. 1990. Arquad 3.16: Determination of Physico-Chemical Properties. Report number 90/AKL013/0587. Akzo Chemicals International, BV, The Netherlands.

Other

Last changed: May 14, 2001

Order number for sorting: 30

Remarks:

3.1.1 Photodegradation

Test Substance

Identity:	Dihydrogenatedtallow dimethyl ammonium chloride (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	Silica gel adsorption and irradiation
GLP:	Not stated
Year:	Not stated
Light Source:	1. Pyrex-filtered UV light 2. quartz-filtered UV light
Light Spectrum:	UV
Relative Intensity:	Not stated
Spectrum of Substance:	Not stated
Remarks:	

Results

Concentration of Substance:	Not stated
Temperature:	Not stated
Direct Photolysis:	Not stated
Oxygen radicals reaction:	Not stated
Ozone Reaction:	Not stated
Indirect Photolysis:	After 72 hours of Pyrex-filtered UV light, 43% of the test substance had been degraded (Disulfine Blue Active Substance (DBAS) response). Ten days after a 16 hour quartz-filtered UV light exposure, 63% DOC disappearance occurred using the OECD screening biodegradation test but no change occurred in the DBAS response.
Breakdown products:	Not stated
Remarks:	The authors of the study considered that only part of the decomposition products obtained from the quartz-filtered UV exposure of the test substance can be used by bacteria as a source of carbon. Products obtained from the Pyrex-filtered UV exposure were largely and rapidly biodegraded, reaching 81% mineralization after 28 days. The DBAS response disappeared after 10 days.

Conclusions	The results of the test provide some evidence of photodegradation of the test substance.
Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	2D
Remarks:	Reliable with restrictions; information provided in ECETOC technical report.

References	European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). 1993. DHTDMAC: Aquatic and Terrestrial Hazard Assessment. CAS RN 61789-80-8. Technical Report number 53, ISSN-0773-8072-53. ECETOC, Brussels, Belgium.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	20c
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Dodecyltrimethylammonium chloride (CAS RN 112-00-5; Ammonium, dodecyltrimethyl-, chloride)
Purity:	No information provided
Remarks:	

Method

Method/Guideline followed:	Non-guideline study of the affect of sediment concentration on biodegradation of the test substance.
Test Type:	Aerobic biodegradation
GLP:	No
Year:	1986
Contact Time:	1 – 250 hours
Inoculum:	Resident bacteria in river water
Remarks:	Slurries of autoclaved river sediment and water (0 to 500 g/l) were spiked with radiolabeled test substance (20 to 200 µg/l) and placed in centrifuge tubes. Tubes were shaken at 200 rpm. Duplicate samples were removed from the shaker at different time intervals (1 to 250 hours) and analyzed for $^{14}CO_2$ and ^{14}C-test substance.

Results

Degradation:	The extent of biodegradation was related to the concentration of sediment present in the sediment/water slurries. It ranged from 0% to approximately 35% in 250 hours.
Results:	The results indicate that a sediment-level threshold exists above which the rate and extent of degradation decreases.
Kinetic:	No information provided
Breakdown Products:	No information provided
Remarks:	The results support a previous study that aqueous-phase test substance can be biodegraded and the fraction adsorbed to sediment particles is unavailable for degradation.

Conclusions	Evidence is provided of the aerobic biodegradability of dodecyltrimethylammonium chloride.
Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability: 2D

Remarks: Reliable with restrictions; summary report of non-guideline research project.

References

Shimp, R. J. 1986. Project Summary: Effects of Sediment Concentration on Biodegradation in Aquatic Sediments. Document ID number. 86-870001367. Procter & Gamble Co., Cincinnati, OH, U. S.

Other Available Reports

Shimp, R. J. and R. L. Young. Availability of Organic Chemicals for Biodegradation in Settled Bottom Sediments. Document ID number 86-870001366. Procter & Gamble Co., Cincinnati, Ohio.
2A: Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

Other

Last Changed: December 13, 2001

Order number for Sorting: 2

Remarks:

3.5 Biodegradation

Test Substance

Identity:	Ammonium, dodecyltrimethyl-, chloride, (CAS RN 112-00-5)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	No specific method/guideline was cited, but the report described a shake-flask biodegradation method.
Test Type:	Aerobic biodegradation
GLP:	No
Year:	1974
Contact Time:	48 hours
Inoculum:	Mixed microbial culture originating from raw city sewage that grew in a mineral salts solution.
Remarks:	Biodegradation tests were carried out in 250-ml Erlenmeyer flasks at 25 °C on a gyratory shaker. Treatments consisted of (1) inoculated blank media, (2) uninoculated media containing the test substance, and (3) inoculated media containing the test substance. Biodegradation was based on disappearance of test substance over time. Test substance concentrations were measured using a colorimetric analytical method for the detection of the test substance.

Results

Degradation:	The test substance was biodegraded 98.3% by 48 hours.
Results:	The test substance was found to be biodegradable at concentrations equal to or less than 10 mg/l.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	Although this study reported a high biodegradation rate, removal by adsorption to surfaces and/or particles may have affected the results.

Conclusions

Remarks:	Cationic substances spontaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and other organic materials. Therefore, results from this study must be interpreted with caution (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	2B
Remarks:	Reliable with restrictions; basic data given, comparable to guidelines/standards.

References

Andrews, C. L. and A. M. Tenny. 1974. Evaluation of Biodegradability of Amines and Quaternary Ammonium Compounds at Low Concentrations. Tenco Hydro/Aerosciences, Inc., Countryside, IL, U. S.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	2a
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Ammonium, hexadecyltrimethyl-, chloride, (CAS RN 112-02-7)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	No specific method/guideline was cited, but the report described a shake-flask biodegradation method.
Test Type:	aerobic biodegradation
GLP:	No
Year:	1974
Contact Time:	48 hours
Inoculum:	Mixed microbial culture originating from raw city sewage that grew in a mineral salts solution.
Remarks:	Biodegradation tests were carried out in 250-ml Erlenmeyer flasks at 25°C on a gyratory shaker. Treatments consisted of (1) inoculated blank media, (2) uninoculated media containing the test substance, and (3) inoculated media containing the test substance. Biodegradation was based on disappearance of test substance over time. Test substance concentrations were measured using a colorimetric analytical method for the detection of the test substance.

Results

Degradation:	The test substance was biodegraded 81.9% by 48 hours.
Results:	The test substance was found to be biodegradable at concentrations equal to or less than 10 mg/l.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	Although this study reported a high biodegradation rate, removal by adsorption to surfaces and/or particles may have affected the results.

Conclusions

Remarks	Cationic substances spontaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and other organic materials. Therefore, results from this study must be interpreted with caution (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	2B
Remarks:	Reliable with restrictions; basic data given, comparable to guidelines/standards.

References

Andrews, C. L. and A. M. Tenny. 1974. Evaluation of Biodegradability of Amines and Quaternary Ammonium Compounds at Low Concentrations. Tenco Hydro/Aerosciences, Inc., Countryside, IL, U. S.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	3a
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Arquad 16-29 (CAS RN 112-02-7; Ammonium, hexadecyltrimethyl-, chloride)
Purity:	29.4%
Remarks:	

Method

Method/Guideline followed:	OECD Guidelines for Testing of Chemicals, Guideline No. 301D: Closed Bottle Test.
Test Type:	Aerobic ready biodegradability
GLP:	Yes
Year:	1993
Contact Time:	42 days
Inoculum:	Activated sludge
Remarks:	The experiment measured the biodegradability of the test substance in the Closed Bottle Test. Prior to the start of the test, activated sludge was collected and preconditioned by aerating a sludge suspension in dilution water (200 mg dry weight (d.w.)/l) for a period of one week. The sludge was diluted to a concentration of 2 mg d.w./l in the test. Solutions of the test substance were prepared to achieve a concentration of 6.7 mg test substance/l. The theoretical oxygen demand (ThOD) of the test substance was 0.85 g O_2/g. Sodium acetate was used as a reference compound. At test initiation, glass 280-ml BOD bottles were filled completely with a suspension of preconditioned activated sludge in dilution water and the target concentration of the test or reference substance. Silica gel was used to reduce the concentration of the test substance in the water phase. Dissolved oxygen measurements were carried out in duplicate BOD bottles on days 0, 7, 14, 21, and 28. The test was prolonged to 42 days by measuring the dissolved oxygen in the day 28 bottles on days 35 and 42 using a special funnel to extract and replace the test solution. Biodegradation was calculated as the percent ratio of BOD/ThOD.

Results

Degradation:	The test substance was biodegraded by 65% at day 28 and 75% at day 42.
Results:	Based on the percent biodegradation, the test substance was classified as readily biodegradable.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	The validity of the test was demonstrated by an endogenous respiration of 0.95 mg/l at day 28, differences between replicate dissolved oxygen measurements of < 20%, and a biodegradation of 77% by day 14 for the reference compound.

Conclusions	The test substance is readily biodegradable.
Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	1A
Remarks:	Reliable without restriction, guideline study (OECD)

References	Van Ginkel, C. G. and C. A. Stroo. 1993. Biodegradability of Arquad 16-29 in the Closed Bottle Test. Report number. CRL F93001. Akzo Research Laboratories, Arnhem, The Netherlands.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	3b
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Arquad 16-29 (CAS RN 112-02-7; Ammonium, hexadecyltrimethyl-, chloride)
Purity:	29.4%
Remarks:	

Method

Method/Guideline followed:	OECD Guidelines for Testing of Chemicals, Guideline No. 301D: Closed Bottle Test.
Test Type:	Aerobic ready biodegradability
GLP:	Yes
Year:	1990
Contact Time:	56 days
Inoculum:	Activated sludge
Remarks:	The experiment measured the biodegradability of the test substance in the Closed Bottle Test. Prior to the start of the test, activated sludge was collected and preconditioned by aerating a sludge suspension in dilution water (200 mg dry weight (d.w.)/l) for a period of one week. The sludge was diluted to a concentration of 2 mg d.w./l in the test. Solutions of the test substance were prepared to achieve a concentration of 2.0 mg test substance/l. The theoretical oxygen demand (ThOD) of the test substance was 2.9 g O_2/g. Sodium acetate was used as a reference compound. At test initiation, glass 280-ml BOD bottles were filled completely with a suspension of preconditioned activated sludge in dilution water and the target concentration of the test or reference substance. Silica gel was used to reduce the concentration of the test substance in the water phase. Dissolved oxygen measurements were carried out in duplicate BOD bottles on days 0, 5, 15, and 28. The test was prolonged to 56 days by measuring the dissolved oxygen in the day 28 bottles on days 42 and 56 using a special funnel to extract and replace the test solution. Biodegradation was calculated as the percent ratio of BOD/ThOD.

Results

Degradation:	The test substance was biodegraded by 48% at day 28 and 60% at day 56.
Results:	Based on the percent biodegradation, the test substance was classified as biodegradable although it failed the criteria for ready biodegradability.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	The validity of the test was demonstrated by an endogenous respiration of 0.5 mg/l and the total mineralization of the reference compound.

Conclusions

Remarks:	Cationic substances spontaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and other organic materials. Therefore, results from this study must be interpreted with caution (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	1A
Remarks:	Reliable without restriction, guideline study (OECD)

References Van Ginkel, C. G. 1990. Biodegradability of Arquad 16-29. Report number CRL F90189. Akzo Research Laboratories, Arnhem, The Netherlands.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	3c
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Quaternary ammonium compounds, trimethyltallow alkyl, chlorides (CAS RN 8030-78-2; Quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	No specific method/guideline was cited, but the report described a shake-flask biodegradation method.
Test Type:	Aerobic biodegradation
GLP:	No
Year:	1974
Contact Time:	48 hours
Inoculum:	Mixed microbial culture originating from raw city sewage that grew in a mineral salts solution.
Remarks:	Biodegradation tests were carried out in 250-ml Erlenmeyer flasks at 25°C on a gyratory shaker. Treatments consisted of (1) inoculated blank media, (2) uninoculated media containing the test substance and (3) inoculated media containing the test substance. Biodegradation was based on disappearance of test substance over time. Test substance concentrations were measured using a colorimetric analytical method for the detection of the test substance.

Results

Degradation:	The test substance was biodegraded 95.3% by 48 hours.
Results:	The test substance was found to be biodegradable at concentrations equal to or less than 10 mg/l.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	Although this study reported a high biodegradation rate, removal by adsorption to surfaces and/or particles may have affected the results.

Conclusions

Remarks:	Cationic substances spontaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and other organic materials. Therefore, results from this study must be interpreted with caution (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability: 2B

Remarks: Reliable with restrictions; basic data given, comparable to guidelines/standards.

References

Andrews, C. L. and A. M. Tenny. 1974. Evaluation of Biodegradability of Amines and Quaternary Ammonium Compounds at Low Concentrations. Tenco Hydro/Aerosciences, Inc., Countryside, IL, U. S.

Other Available Reports

Other

Last Changed: December 13, 2001

Order number for Sorting: 10a

Remarks:

3.5 Biodegradation

Test Substance

Identity:	Tallow trimethylammonium chloride (CAS RN 8030-78-2; Quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	50.5%
Remarks:	

Method

Method/Guideline followed:	OECD Guidelines for Testing of Chemicals, Guideline No. 301D: Closed Bottle Test.
Test Type:	Aerobic ready biodegradability
GLP:	Yes
Year:	1993
Contact Time:	35 days
Inoculum:	Activated sludge
Remarks:	The experiment measured the biodegradability of the test substance in the Closed Bottle Test. Prior to the start of the test, activated sludge was collected and preconditioned by aerating a sludge suspension in dilution water (200 mg dry weight (d.w.)/l) for a period of one week. The sludge was diluted to a concentration of 2 mg d.w./l in the test. Solutions of the test substance were prepared to achieve a concentration of 4.0 mg test substance/l. The theoretical oxygen demand (ThOD) of the test substance was 2.3 mg O_2/mg. Sodium acetate was used as a reference compound. At test initiation, glass 280-ml BOD bottles were filled completely with a suspension of preconditioned activated sludge in dilution water and the target concentration of the test or reference substance. Silica gel was used to reduce the concentration of the test substance in the water phase. Dissolved oxygen measurements were carried out in duplicate BOD bottles on days 7, 14, 21, and 28. The test was prolonged to 35 days by measuring the dissolved oxygen in the day 28 bottles using a special funnel to extract and replace the test solution. Biodegradation was calculated as the percent ratio of BOD/ThOD.

Results

Degradation:	The test substance was biodegraded by 48% by day 28 and 51% by day 35.
Results:	The percent degradation indicates that the test substance is biodegradable, although it failed to meet the conditions of ready biodegradable.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	The validity of the test was demonstrated by an endogenous respiration of 0.95 mg/l at day 28, differences between replicate dissolved oxygen measurements of < 20%, and a biodegradation of 77% by day 14 for the reference compound.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	1A
Remarks:	Reliable without restriction; guideline study (OECD).

References Van Ginkel, C. G. and C. A. Stroo. 1993. Biodegradability of Arquad T-50 in the Closed Bottle Test. Report number CRL F93002. Akzo Research Laboratories, Arnhem, The Netherlands.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	10b
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Arquad T-30 (CAS RN 8030-78-2; Quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	30%
Remarks:	

Method

Method/Guideline followed:	OECD Guidelines for Testing of Chemicals, Guideline No. 301D: Closed Bottle Test.
Test Type:	Aerobic ready biodegradability
GLP:	Yes
Year:	1990
Contact Time:	56 days
Inoculum:	Activated sludge
Remarks:	The experiment measured the biodegradability of the test substance in the Closed Bottle Test. Prior to the start of the test, activated sludge was collected and preconditioned by aerating a sludge suspension in dilution water (200 mg dry weight (d.w.)/l) for a period of one week. The sludge was diluted to a concentration of 2 mg d.w./l in the test. Solutions of the test substance were prepared to achieve a concentration of 2.0 mg test substance/l. The theoretical oxygen demand (ThOD) of the test substance was 2.6 g O_2/g. Sodium acetate was used as a reference compound. At test initiation, glass 280-ml BOD bottles were filled completely with a suspension of preconditioned activated sludge in dilution water and the target concentration of the test or reference substance. Silica gel was used to reduce the concentration of the test substance in the water phase. Dissolved oxygen measurements were carried out in duplicate BOD bottles on days 5, 15, and 28. The test was prolonged to 56 days by measuring the dissolved oxygen in the day 28 bottles on days 42 and 56 using a special funnel to extract and replace the test solution. Biodegradation was calculated as the percent ratio of BOD/ThOD.

Results

Degradation:	The test substance was biodegraded by 53% by day 28 and 79% by day 56.
Results:	The percent degradation indicates that the test substance is biodegradable, although it failed to meet the conditions of ready biodegradable.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	The validity of the test was demonstrated by oxygen consumption in the bottle with reference compound and an endogenous respiration of 0.5 mg/l. The pH of the medium at day 28 was 7.4.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	1A
Remarks:	Reliable without restriction, guideline study (OECD)

References

Van Ginkel, C. G. 1990. Biodegradability of Arquad T-30. Report number CRL F90188. Akzo Research Laboratories, Arnhem, The Netherlands.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	10c
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Arquad T/50 (CAS RN 8030-78-2; Quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	51.1%
Remarks:	

Method

Method/Guideline followed:	OECD Guidelines for Testing of Chemicals, Guideline No. 301D: Closed Bottle Test.
Test Type:	Aerobic ready biodegradability
GLP:	Yes
Year:	1987
Contact Time:	42 days
Inoculum:	Activated sludge
Remarks:	The experiment measured the biodegradability of the test substance in the Closed Bottle Test. Prior to the start of the test, activated sludge was collected and preconditioned by aerating a sludge suspension in dilution water (1 g suspended solids (s.s.)/l) for a period of one week. The sludge was diluted to a concentration of 3 mg s.s./l in the test. Solutions of the test substance were prepared to achieve a concentration of 2.6 mg test substance/l, which corresponded to a COD of 4.59 mg O_2/l. At test initiation, dark glass 280-ml BOD bottles were filled completely with a suspension of preconditioned activated sludge in dilution water and the target concentration of the test substance. The test was carried out in triplicate and at every O_2 measurement time, a new series of three BOD bottles were sampled. A toxicity assessment treatment was included to measure the potential of the test substance to inhibit the bacterial microflora. The toxicity control included BOD bottles containing two concentrations of test substance and sodium acetate as the reference biodegradable material. Dissolved oxygen concentrations were measured in each bottle on days 0, 14, 28, and 42 using an oxygen electrode. Biodegradation was calculated as the percent ratio of BOD/COD.

Results

Degradation:	The extent of biodegradation achieved 40% after 14 and 28 days and 61% after 42 days.
Results:	Biodegradation of 40% at day 28 and 61% at day 42, suggests that the test substance was not readily biodegradable, but could be considered inherently biodegradable according to OECD recommendations.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	The toxicity control indicated that the test substance was not inhibitory to the inoculum.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	1A
Remarks:	Reliable without restriction; guideline study (OECD)

References

Balk, F. and E. E. Hantink-De Rooij. 1987. Biodegradability of a number of Nitrogen Derivatives (MU-30, Akzo Chemie). Report number D 87/16/0525B. Akzo Laboratories, Arnhem, Holland.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	10d
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Trimethyloctadecylammonium chloride (CAS RN 112-03-8)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	No specific method/guideline was cited, but the report described a shake-flask biodegradation method.
Test Type:	Aerobic biodegradation
GLP:	No
Year:	1974
Contact Time:	48 hours
Inoculum:	Mixed microbial culture originating from raw city sewage that grew in a mineral salts solution.
Remarks:	Biodegradation tests were carried out in 250-ml Erlenmeyer flasks at 25°C on a gyratory shaker. Treatments consisted of (1) inoculated blank media, (2) uninoculated media containing the test substance, and (3) inoculated media containing the test substance. Biodegradation was based on disappearance of test substance over time. Test substance concentrations were measured using a colorimetric analytical method for the detection of the test substance.

Results

Degradation:	The test substance was biodegraded 98.4% by 48 hours.
Results:	The test substance was found to be biodegradable at concentrations equal to or less than 10 mg/l.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	Although this study reported a high biodegradation rate, removal by adsorption to surfaces and/or particles may have affected the results.

Conclusions

Remarks	Cationic substances spontaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and other organic materials. Therefore, results from this study must be interpreted with caution (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	2B
Remarks:	Reliable with restrictions; basic data given, comparable to guidelines/standards.

References

Andrews, C. L. and A. M. Tenny. 1974. Evaluation of Biodegradability of Amines and Quaternary Ammonium Compounds at Low Concentrations. Tenco Hydro/Aerosciences, Inc., Countryside, IL, U. S.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	8a
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides (CAS RN 61789-77-3)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	No specific method/guideline was cited, but the report described a shake-flask biodegradation method.
Test Type:	Aerobic biodegradation
GLP:	No
Year:	1974
Contact Time:	48 hours
Inoculum:	Mixed microbial culture originating from raw city sewage that grew in a mineral salts solution.
Remarks:	Biodegradation tests were carried out in 250-ml Erlenmeyer flasks at 25°C on a gyratory shaker. Treatments consisted of (1) inoculated blank media, (2) uninoculated media containing the test substance, and (3) inoculated media containing the test substance. Biodegradation was based on disappearance of test substance over time. Test substance concentrations were measured using a colorimetric analytical method for the detection of the test substance.

Results

Degradation:	The test substance was biodegraded 80.3% by 48 hours.
Results:	The test substance was found to be biodegradable at concentrations equal to or less than 10 mg/l.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	Although this study reported a high biodegradation rate, removal by adsorption to surfaces and/or particles may have affected the results.

Conclusions

Remarks:	Cationic substances spontaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and other organic materials. Therefore, results from this study must be interpreted with caution (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	2B
Remarks:	Reliable with restrictions; basic data given, comparable to guidelines/standards.

References

Andrews, C. L. and A. M. Tenny. 1974. Evaluation of Biodegradability of Amines and Quaternary Ammonium Compounds at Low Concentrations. Tenco Hydro/Aerosciences, Inc., Countryside, IL, U. S.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	17b
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Arquad 2C-75 (CAS RN 61789-77-3; Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides)
Purity:	76.4%
Remarks:	

Method

Method/Guideline followed:	OECD Guidelines for Testing of Chemicals; Guideline No. 301D: Ready biodegradability, Closed bottle test, and EEC Guideline No. C.6. Degradation-biotic degradation: Closed bottle test.
Test Type:	Aerobic ready biodegradability
GLP:	Yes
Year:	1990
Contact Time:	84 days
Inoculum:	Activated sludge
Remarks:	The experiment measured the biodegradability of the test substance in the Closed Bottle Test. Prior to the start of the test, activated sludge was collected and preconditioned by aerating a sludge suspension in dilution water (200 mg dry weight (d.w./l) for a period of one week. The sludge was diluted to a concentration of 2 mg d.w./l in the test. Solutions of the test substance were prepared to achieve a concentration of 2.6 mg test substance/l. The test material had a theoretical oxygen demand of 2.6 g O_2/g. Because the test substance may be toxic to the inoculum, the test substance was tested in the presence of silica gel to reduce the concentration in the water phase. Sodium acetate was used as a reference substance. In the treatments with test substance alone, dissolved oxygen concentrations were measured in each bottle on days 5, 15, 28, 42, 70, 98, 126, 182 and 214. In the bottles containing test substance and silica gel, dissolved oxygen was measured on days 5, 15, 28, 42, 56, and 84. Dissolved oxygen measurements were made using an oxygen electrode. Biodegradation was calculated as the percent ratio of BOD/ThOD.

Results

Degradation:	In the experiment without silica gel the results were 0% degradation by day 28 and 56% degradation by day 214. In the experiment with silica gel the results were 9% degradation by day 28 and 3% degradation by day 84.
Results:	The degradation results indicate that the test substance is not readily biodegradable.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	The validity of the test was demonstrated by oxygen consumption in the reference substance treatment and endogenous respiration of 0.4 and 0.5 mg/l. The pH values of the medium at day 28 were 7.0 and 7.3.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	1A
Remarks:	Reliable without restriction; guideline study (OECD)

References

Van Ginkel, C. G. 1990. Biodegradability of Arquad 2C-75. Report number CRL F90164. Akzo Research Laboratories, Arnhem, The Netherlands.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	17c1
Remarks:	

3.5 Biodegradation

Test Substance

Identity: Dihydrogenatedtallow dimethyl ammonium chloride (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)

Purity: Not stated

Remarks:

Method

Method/Guideline followed: Studies using various methods/guidelines were reported in the technical report.

Test Type: Both ready biodegradability tests of the BOD and CO_2 evolution types were reported in the technical report.

GLP: Not stated

Year: 1983 - 1987

Contact Time: 33 - 70 days

Inoculum: Inocula from activated sludge sewage treatment plants were almost always used. Some tests reported used adapted or nonadapted inocula.

Remarks:

Results

Degradation: Summary of ready biodegradability BOD tests:

Test	Material	Adapted biomass	Duration (days)	Results (%)	Reference
CO_2	DHTDMAC	No	49	2.8	Procter and Gamble. 1974 – 1986
		No	26	4.8	Procter and Gamble. 1974 – 1986
		No		2.3	Procter and Gamble. 1974 – 1986
BOD	DHTDMAC	No	28	0	Baleux and Caumette. 1977
		Yes	20	19	Clancy and Tanner. 1991
		No	20	8	Clancy and Tanner. 1991
		No	20	12	Clancy and Tanner. 1991
		No	20	17	Clancy and Tanner. 1991
		No	20	35	Clancy and Tanner. 1991

Results: See above

Kinetic: Not stated

Breakdown Products: Not stated

Remarks: Conclusions of all tests (ready and inherent biodegradation) indicate that the test substance is not readily biodegradable as defined by OECD criteria. However, the test substance is amenable to complete mineralization. Biodegradation is slow, but adaptation of the microbial biomass greatly increases the biodegradation rate.

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability: 2D

Remarks: Reliable with restrictions, information provided in an ECETOC technical report.

References

European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). 1993. DHTDMAC: Aquatic and Terrestrial Hazard Assessment. CAS RN 61789-80-8. Technical Report number 53, ISSN-0773-8072-53. ECETOC, Brussels, Belgium.

Baleux, B. and P. Caumette. 1977. Biodegradation de Quelques Agents de Surface Cationiques. Water Research. 11:833 – 841.

Clancy, S. F. and D. A. Tanner. 1991. Determination of Surfactant Biodegradability. Sherex Internal Data. Sherex Chemical Co., Inc., Dublin, OH, U. S.

Larson, R. J. and R. D. Vashon. 1983. Adsorption and Biodegradation of Cationic Surfactants in Laboratory and Environmental Systems. Dev. Ind. Microbiol. 24:425.

Procter & Gamble. 1974 – 1986. As supplied to the ECETOC Task Force on DHTDMAC 1992. Data Available Upon Request from Procter & Gamble European Technical Centre, Professional and Regulatory Services, Brussels, Belgium.

Schoeberl, P., K. J. Bock and L. Huber. 1988. Oekologisch Relevante Daten von Tensiden in Wasch- und Reinigungsmitteln. Tenside Surf. Det. 25:86 – 98.

Van Ginkel, C. G. and C. A. Stroo. 1991. Biodegradability of ARQUAD 2.18. Akzo Technical Report. Akzo Chemical International BV, Amersfoort, The Netherlands.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	20c
Remarks:	

3.5 Biodegradation

Test Substance

Identity:	Quaternary ammonium compounds, bis (hydrogenated tallow alkyl) dimethyl chloride, (CAS RN 61789-80-8)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	No specific method/guideline was cited, but the report described a shake-flask biodegradation method.
Test Type:	Aerobic biodegradation
GLP:	No
Year:	1974
Contact Time:	48 hours
Inoculum:	Mixed microbial culture originating from raw city sewage that grew in a mineral salts solution.
Remarks:	Biodegradation tests were carried out in 250-ml Erlenmeyer flasks at 25 °C on a gyratory shaker. Treatments consisted of (1) inoculated blank media, (2) uninoculated media containing the test substance, and (3) inoculated media containing the test substance. Biodegradation was based on disappearance of test substance over time. Test substance concentrations were measured using a colorimetric analytical method for the detection of the test substance.

Results

Degradation:	The test substance was biodegraded 78.8% by 48 hours.
Results:	The test substance was found to be biodegradable at concentrations equal to or less than 10 mg/l.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	Although this study reported a high biodegradation rate, removal by adsorption to surfaces and/or particles may have affected the results.

Conclusions

Remarks:	Cationic substances spontaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments, and other organic materials. Therefore, results from this study must be interpreted with caution (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	2B
Remarks:	Reliable with restrictions; basic data given, comparable to guidelines/standards.

References

Andrews, C. L. and A. M. Tenny. 1974. Evaluation of Biodegradability of Amines and Quaternary Ammonium Compounds at Low Concentrations. Tenco Hydro/Aerosciences, Inc., Countryside, IL, U. S.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	21a
Remarks:	

3.5 BIODEGRADATION

Test Substance

Identity: Arquad 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)

Purity: 86%

Remarks:

Method

Method/Guideline followed: OECD Guideline 301D, Ready Biodegradability: Closed Bottle Test; EEC 1984, Degradation-biotic Degradation: Closed Bottle Test

Test type: Ready biodegradability, closed bottle test

GLP: Yes

Year: 1990

Contact time: 28 days

Inoculum: Activated sludge

Remarks: The test substance was added to an aqueous solution of mineral salts and exposed to relatively low numbers of microorganisms under aerobic conditions for a period of 28 days. Activate sludge taken from a SCAS unit on days 0, 32 and 91, was used as an inoculum. Because the test substance was poorly soluble in water, it first was dissolved in dichloromethane. The test substance in dichloromethane was added to silica gel. The solvent was allowed to evaporate and the entire contents then were transferred to the BOD bottle. Although no additional oxygen consumption was expected, controls with silica gel were carried out as well. A reference compound was not used in this test. The closed bottles were incubated at 20 ºC.

Results

Degradation: No biodegradation of the test substance was observed; therefore, the test substance may have been removed from the wastewater by adsorption. This adsorption was very efficient and the test substance adsorbed did not influence the performance of the wastewater purification plant.

Results: See below

Kinetic: **Inoculated with sludge from the SCAS test (day 0)**

Time (days)	10	24	45	58	91	119
Oxygen consumption (mg 0_2/l)	0.0	0.0	0.0	0.0	0.1	0.0
Biodegradation (%BODD/ThOD)	0	0	0	0	2	0

Inoculated with sludge from the SCAS test (day 32)

Time	13	26	59	87
Oxygen consumption ($mg\ 0_2/l$)	0.0	0.0	0.0	0.1
Biodegradation (%BODD/ThOD)	0	0	0	2

Inoculated with sludge from the SCAS test (day 91)

Time	5	32	80
Oxygen consumption ($mg\ 0_2/l$)	0.0	0.1	0.0
Biodegradation (%BODD/ThOD)	0	2	0

Breakdown products: Not stated
Remarks:

Conclusions

Remarks: Closed bottle tests with sludge from the SCAS test as inoculum show that the test substance is not biodegradable under aerobic conditions. (Author of report)
The biodegradation of Arquad 3.16 has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1A
Remarks: Reliable without restriction; guideline study.

References

Van Ginkel, C. G. and C. A. Stroo. 1990. Biodegradability of Arquad 3.16 in the SCAS Test. Study number T89-09-03.1. Akzo Research Laboratories Arnhem, The Netherlands.

Other

Last changed: May 14, 2001
Order number for sorting: 35CB
Remarks:

3.5 Biodegradation

Test Substance

Identity:	Arquad 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	86%
Remarks:	

Method

Method/Guideline followed:	OECD Guideline 302A, Inherent Biodegradability: Modified SCAS Test; EEC 1988, Biodegradability Modified SCAS Test
Test type:	Aerobic inherent biodegradability
GLP:	Yes
Year:	1990
Contact time:	90 Days
Inoculum:	Activated sludge
Remarks:	A solution of the test substance in ethanol, which was diluted in deionized water, was exposed to relatively high concentrations of microorganisms maintained by daily addition of primary settled sewage. A control with ethanol was included in the test. The test was conducted at an influent concentration of the test compound of 2 mg TOC/l for a period of 90 days. SCAS units were fed primary settled sewage without test substance daily for seven days. On day 7, individual settled sludges were mixed and sludge from the resulting composite was added to SCAS units. The test substance stock solution (5 ml) was added to test units containing primary settled sewage and concentrated phosphate buffer. After 23 hours aeration, the sludge was allowed to settle for 45 minutes and the supernatant drawn off and analyzed for total organic carbon content. The fill and draw procedure was repeated six times per week throughout the test. Only at the start of the test was the TOC in the supernatant liquor determined daily. A less frequent analysis was performed in the later period of the test. The test was performed at 20ºC. The pH of the mixed liquor in the SCAS units was maintained at 7.0 by daily addition of a concentrated phosphate buffer.

Results

Degradation:	The test substance was totally removed from the wastewater in the SCAS test, either due to the adsorption on the sludge or biodegradation.
Results:	After the addition of the test substance on day 7, the removal of Arquad 3.16 was accomplished immediately

due to the adsorption of the sludge or biodegradation. The TOC values of the units did not increase due to the adsorption of the sludge or biodegradation of Arquad 3.16.

Kinetic: Percent removal was 90% by day 10 and 100% by day 12.

TOC Concentrations in the Effluent of the SCAS units (mg/l)			
Time (hours)	**Control**	**Ethanol**	**Arquad 3.16**
6	11	16	16
7[a]	10	11	14
11	9	14	11
14	10	9	10
20	9	11	9
29	7	7	7
36	7	7	6
43	8	9	7
46	8	9	7
56	11	9	8
77	8	8	8
91	6	7	6

[a] First addition of test material

Breakdown products: None
Remarks:

Conclusions
Remarks: The biodegradation of Arquad 3.16 has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality
Reliability (Klimisch): 1A
Remarks: Reliable without restriction; guideline study.

References

Van Ginkel, C. G. and C. A. Stroo. 1990. Biodegradability of Arquad 3.16 in the SCAS Test. Study number T89-09-03.1. Akzo Research Laboratories Arnhem, The Netherlands.

Other
Last changed: May 12, 2001
Order number for sorting: 35SCAS
Remarks:

3.5 Biodegradation

Test Substance

Identity:	Fatty amine derivative (CAS RN 68607-29-4; Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichloride)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	OECD Guidelines for Testing of Chemicals, Guideline 301D: Ready Biodegradability, Closed Bottle Test. Also conformed to EEC Method C.6., Degradation-biotic degradation: Closed bottle test.
Test Type:	Aerobic ready biodegradability
GLP:	Yes
Year:	1990
Contact Time:	182 days
Inoculum:	Activated sludge
Remarks:	The experiment measured the biodegradability of the test substance in the Closed Bottle Test. Prior to the start of the test, activated sludge was collected and preconditioned by aerating a sludge suspension in dilution water (200 mg dry weight (d.w./l) for a period of one week. The sludge was diluted to a concentration of 2 mg d.w./l in the test. Solutions of the test substance were prepared to achieve a concentration of 2.0 mg test substance/l. The test material had a theoretical oxygen demand of 2.5 g O_2/g. Because the test substance may be toxic to the inoculum, the test substance was tested in the presence of silica gel to reduce the concentration in the water phase. Sodium acetate was used as a reference substance. In the treatments with test substance alone, dissolved oxygen concentrations were measured in each bottle on days 5, 15, 28, 42, 70, 98, 126, and 182. In the bottles containing test substance and silica gel, dissolved oxygen was measured on days 5, 15, 28, 42, 70, and 98. Dissolved oxygen measurements were made using an oxygen electrode. Biodegradation was calculated as the percent ratio of BOD/ThOD.

Results

Degradation:	The treatment containing the test substance alone did not show any biodegradation. The treatment containing the test substance with silica gel showed biodegradation of 12%.
Results:	The percentage of biodegradation indicated that the test substance is not readily biodegradable in the closed bottle test.
Kinetic:	Not stated
Breakdown Products:	Not stated
Remarks:	The validity of the test was demonstrated by oxygen consumption in the bottles with sodium acetate and endogenous respiration rates of 0.1 and 0.5 mg/l. The pH of the media at day 28 was 7.4 and 6.8.

Conclusions The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability:	1A
Remarks:	Reliable without restrictions; guideline study (OECD)

References Van Ginkel, C. G. 1990. Biodegradability of [CAS RN 68607-29-4]. Report number CRL F90177. Akzo Research Laboratory, Arnhem, The Netherlands.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	23a
Remarks:	

4.1 Acute/Prolonged Toxicity to Fish

Test Substance

Identity:	Ammonium, docecyltrimethyl-chloride (CAS RN 112-00-5)
Purity:	50%
Remarks:	

Method

Method/guideline followed:	Non-specific test method
Type:	Static acute
GLP:	No
Year:	1972
Species/Strain/Supplier:	Atlantic salmon (*Salmo salar*)/NA/St. John Fish Culture Station
Analytical Monitoring:	No
Exposure Period:	96 hours
Statistical Methods:	Not stated
Remarks:	Fish used in testing ranged from 8.2 to 11.7 cm in length and weighed 5.1 – 14.1 g. Concentrations used in testing were corrected for active ingredient content.

Results

Nominal concentrations (mg/l):	Not stated
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
Element Value:	96-hour LC_{50} = 6.0 mg/l
Statistical Results:	96-hour LC_{50} = 6.0 mg/l
Result:	96-hour LC_{50} = 6.0 mg/l
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2B
Remarks:	Reliable with restrictions; basic data given, comparable to guidelines/standards.

References

Wildish, D. J. and W. G. Carson. 1972. Acute Lethality of Some Nonionic and Cationic Surfactants to *S. salar and G. oceanicus*. Fisheries Research Board of Canada, Manuscript Report Series number 1212.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for sorting:	2b
Remarks:	

4.1 Acute/Prolonged Toxicity to Fish

Test Substance

Identity:	Ammonium, dococyltrimethyl-chloride (CAS RN 112-02-7)
Purity:	50%
Remarks:	

Method

Method/guideline followed:	Non-specific test method
Type:	Static acute
GLP:	No
Year:	1972
Species/Strain/Supplier:	Atlantic salmon (*Salmo salar*)/NA/St. John Fish Culture Station
Analytical Monitoring:	No
Exposure Period:	24 hours
Statistical Methods:	Not stated
Remarks:	Fish used in testing ranged from 8.2 to 11.7 cm in length and weighed 5.1 – 14.1 g. Concentrations used in testing were corrected for active ingredient content.

Results

Nominal concentrations (mg/l):	Not stated
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
Element Value:	24-hour LC_{50} = 0.07 mg/l
Statistical Results:	24-hour LC_{50} = 0.07 mg/l
Result:	24-hour LC_{50} = 0.07 mg/l
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2B
Remarks:	Reliable with restrictions; basic data given, comparable to guidelines/standards.

References

Wildish, D. J. and W. G. Carson. 1972. Acute Lethality of Some Nonionic and Cationic Surfactants to *S. salar and G. oceanicus*. Fisheries Research Board of Canada, Manuscript Report Series number 1212.

Other Available Reports

Other

Last Changed: December 13, 2001
Order number for sorting: 4a
Remarks:

4.1 Acute/Prolonged Toxicity to Fish

Test Substance

Identity:	Trimethyloctadecyl ammonium chloride (CAS RN 112-03-8)
Purity:	50%
Remarks:	

Method

Method/guideline followed:	Non-specific test method
Type:	Static acute
GLP:	No
Year:	1972
Species/Strain/Supplier:	Atlantic salmon (*Salmo salar*)/NA/St. John Fish Culture Station
Analytical Monitoring:	No
Exposure Period:	96 hours
Statistical Methods:	Not stated
Remarks:	Fish used in testing ranged from 8.2 to 11.7 cm in length and weighed 5.1 – 14.1 g. Concentrations used in testing were corrected for active ingredient content.

Results

Nominal concentrations (mg/l):	Not stated
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
Element Value:	96-hour LC_{50} = 0.07 mg/l
Statistical Results:	96-hour LC_{50} = 0.07 mg/l
Result:	96-hour LC_{50} = 0.07 mg/l
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2B
Remarks:	Reliable with restrictions; basic data given, comparable to guidelines/standards.

References

Wildish, D. J. and W. G. Carson. 1972. Acute Lethality of Some Nonionic and Cationic Surfactants to *S. salar and G. oceanicus*. Fisheries Research Board of Canada, Manuscript Report Series number 1212.

Other Available Reports

Other

Last Changed: December 13, 2001
Order number for sorting: 8b
Remarks:

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (DTDMAC); (CAS RN 68783-78-8)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Test procedures followed EPA 1975; Methods for acute toxicity tests with fish, macroinvertebrates and amphibians (EPA 660/3-75-009).
Type:	Static acute
GLP:	No
Year:	1982
Species/Strain/Supplier:	Bluegill/*Lepomis macrochirus*/commercial hatcheries
Analytical Monitoring:	Yes
Exposure Period:	96 hours
Statistical Methods:	Probit analysis or other accepted statistical procedures.
Remarks:	The 96-hour tests were conducted in 20-liter glass aquaria containing 15 liters of test solutions. The test waters were maintained at 19-22°C and were not aerated. Ten fish were exposed to each of five test concentrations and a control in reconstituted water or Town River water (Plymouth County, Massachusetts). Chemical and physical quality of the reconstituted water was as follows: pH 6.5 – 7.3; total harness 131 – 163 mg/l $CaCo_3$; suspended solids 0 mg/l; chlorinated insecticides < 0.005 µg/l; and organophosphates <0.01 µg/l. Chemical and physical quality of the Town River water was as follows: pH 6.4 – 7.7; total harness 14 – 38 mg/l $CaCo_3$; suspended solids 2 – 84 mg/l; chlorinated insecticides < 0.1 µg/l; organophosphates <0.5 µg/l; methylene blue active substances 0.04 – 0.59 mg/l; and disulfine blue active substances 0.01 – 0.015 mg/l. Bluegill ranged from 1.2 to 1.7 g in weight and from 23 to 60 mm in length. Fish were acclimated for 14 to 30 days prior to use in water having physical and chemical characteristics similar to those of the water used in the tests. Fish were fed trout chow daily during acclimation, but were not fed 24 hours to 48 hours prior to and during testing. In an additional test, bluegill were exposed to 10.1 ml/l in river water in conjunction with 0-200 mg/l suspended solids (bottom silt collected from the Town River, Plymouth County, Massachusetts). The LC_{50} values represent nominal concentrations of the active ingredient.

This publication presents data for a number of endpoints and does not specify concentrations used for assay. The value is included in the dataset since it provides information consistent with the data for the category.

Results

Nominal concentrations (mg/l):	Not stated
Measured concentrations (mg/l):	N/A
Unit:	mg/l
Element Value:	96-hour LC_{50}
Statistical Results:	96-hour LC_{50} in reconstituted water ranged from 0.62 to 3.0 mg/l 96-hour LC_{50} in Town River water ranged from 10.1 to >24.0 mg/l
Result:	The addition of suspended solids to Town River water further reduced the bioavailability of the test substance to bluegill exposed to 10.1 mg/l of the test substance. When 20 mg/l of suspended solids were added to the 10.1 mg/l test substance concentration 80% mortality was noted; however; at 50 mg/l of suspended solids and greater, mortality was 0%.
Remarks:	

Conclusions The data are useful in support of the overall category. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch):	2B
Remarks:	Reliable with restriction; basic data given

References

Lewis, M. A. and V. T. Wee. 1983. Aquatic Safety Assessment for Cationic Surfactants. Microbiological Associates, Bethesda, MD, USA. Unpublished report (No. T1806.501).

Other

Last Changed:	November 16, 2001
Order number for sorting:	604
Remarks:	

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (DTDMAC); (CAS RN 68783-78-8)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Test procedures followed EPA 1975; Methods for acute toxicity tests with fish, macroinvertebrates and amphibians (EPA 660/3-75-009).
Type:	Static acute
GLP:	No
Year:	1982
Species/Strain/Supplier:	Sheepshead minnow/(*Cyprinidon variagatus*) /obtained from the Big Lagoon near Pensacola, Florida.
Analytical Monitoring:	Yes
Exposure Period:	96 hours
Statistical Methods:	Mortality data were analyzed by probit analysis.
Remarks:	The test species were acclimated to laboratory test conditions (salinity of 24% and pH of 8.0 ± 0.5) for at least one week before use. Tests were conducted in 19-liter glass aquaria containing 15 liters of filtered, natural seawater. Salinity ranged from 16 to 26% during testing, and the water temperature was maintained at 20 ± 1°C for all tests. Ten sheepshead minnows (15-20 mm) were exposed to each of five test concentrations and the control. Mortality was recorded daily. The LC_{50} values were based on nominal concentrations. This publication presents data for a number of endpoints and does not specify concentrations used for assay. The value is included in the dataset since it provides information consistent with the data for the category.

Results

Nominal concentrations (mg/l):	Not stated
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
Element Value:	96-hour LC_{50}
Statistical Results:	96-hour LC_{50} = 24.0 mg/l (95% confidence limit of 9.5 – 6.3 mg/l)
Remarks:	

Conclusions	The data are useful in support of the overall category. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)
Data Quality	
Reliability (Klimisch):	2B
Remarks:	Reliable with restriction; basic data given
References	Lewis, M. A. and V. T. Wee. 1983. Aquatic Safety Assessment for Cationic Surfactants. Microbiological Associates, Bethesda, MD, USA. Unpublished report (No. T1806.501).
Other	
Last Changed:	November 16, 2001
Order number for sorting:	604 b
Remarks:	

4.1 Acute/Prolonged Toxicity to Fish - Bluegill

Test Substance

Identity:	Arquad 2HT-75 (CAS RN 61789-80-8; Quaternary ammonium compounds, bis (hydrogenated tallow alkyl) dimethyl, chloride)
Purity:	75%
Remarks:	

Method

Method/guideline followed:	Test procedures followed EPA 1975, Methods for acute toxicity tests with fish, macroinvertebrates and amphibians (EPA 660/3-75-00)
Type:	Static acute
GLP:	No
Year:	1977
Species/Strain/Supplier:	Bluegill (*Lepomis macrochirus*)/NA/commercial supplier
Analytical Monitoring:	No
Exposure Period:	96 hours
Statistical Methods:	Spearman-Karber LC_{50} calculations (Finney 1971)
Remarks:	The study measured the acute toxicity of the test substance to bluegill during a 96-hour static exposure period. Fish were maintained in the laboratory until testing. Water used for holding and testing was reconstituted soft deionized well water having approximately the following: temperature 22°C, pH 7.6, total hardness 43 mg/l as $CaCO_3$, total alkalinity 28 mg/l as $CaCO_3$, and specific conductance 180 μmhos/cm. Bluegill at the time of testing were approximately 7 months old and had a mean length of 40 mm and a mean weight of 0.97 g. Forty-eight hours prior to the test, feeding was ceased. Five exposure levels and a control were used in the test. No replication of test levels was used. Test substance was melted in a hot-water bath, weighed and diluted to volume in volumetric glassware with deionized water. Test vessels were 5-gallon glass containers holding 15 liters of test solution. Tests were started by introducing the test substance into the vessels containing dilution water, thoroughly mixing the solutions, then introducing the fish. Ten fish were placed into each test vessel. Fish loading in the test was 0.65 g/l. Observations for deaths and abnormal behavioral effects were made at 24, 48 and 96 hours.

Results

Nominal concentrations (mg/l):	0 (control), 0.56, 1.0, 1.8, 3.2, and 5.6 mg/l
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
Element Value:	96-hour LC_{50}
Statistical Results:	96-hour LC_{50} = 1.33 mg/l (95% confidence interval = 1.07 and 1.65 mg/l)
Result:	Additional results included the following: 24-hour LC_{50} = 2.36 mg/l 48-hour LC_{50} = 1.33 mg/l (95% CI = 1.07 – 1.65) The no effect concentration was 0.56 mg/l.
Remarks:	100% mortality occurred in the 3.2 and 5.6 mg/l treatments, while 80% and 20% mortality occurred at 1.8 and 1.0 mg/l, respectively. No mortality occurred at 0.56 mg/l. Behavioral observations made during the test indicated that bluegill exposed to 1.0 mg/l and higher became disoriented, demonstrated erratic swimming behavior and showed signs of varied discoloration..

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study

References

Dean, W. P. 1977. The Acute Toxicity of Arquad 2HT-75, Dimethyldi (hydrogenated tallow) ammonium chloride 75% active, 1633602, to the Bluegill Sunfish *Lepomis machrochirus Rafinesque* and Rainbow Trout *Salmo gairdneri Richardson*. Study number 398-001. International Research and Development Corporation.

Other Available Reports This report was also summarized for rainbow trout.

Other

Last Changed:	December 13, 2001
Order number for sorting:	17s bluegill
Remarks:	

4.1 Acute/Prolonged Toxicity to Fish – Rainbow Trout

Test Substance

Identity:	Arquad 2HT-75 (CAS RN 61789-80-8; Quaternary ammonium compounds, bis (hydrogenated tallow alkyl) dimethyl, chloride)
Purity:	75%
Remarks:	

Method

Method/guideline followed:	Test procedures followed EPA 1975, Methods for acute toxicity tests with fish, macroinvertebrates and amphibians (EPA 660/3-75-00)
Type:	Static acute
GLP:	No
Year:	1977
Species/Strain/Supplier:	Rainbow trout/NA/commercial supplier
Analytical Monitoring:	No
Exposure Period:	96 hours
Statistical Methods:	Spearman-Karber LC_{50} calculations (Finney 1971)
Remarks:	The study measured the acute toxicity of the test substance to rainbow trout during a 96-hour static exposure period. Fish were maintained in the laboratory until testing. Water used for holding and testing was reconstituted soft deionized well water having approximately the following: temperature 12°C, pH 7.6, total hardness 43 mg/l as $CaCO_3$, total alkalinity 28 mg/l as $CaCO_3$, and specific conductance 180 µmhos/cm. Rainbow trout at the time of testing were approximately 4 months old and had a mean length of 50 mm and a mean weight of 1.08 g. Forty-eight hours prior to the test, feeding was ceased. Five exposure levels and a control were used in the test. No replication of test levels was used. Test substance was melted in a hot-water bath, weighed and diluted to volume in volumetric glassware with deionized water. Test vessels were 5-gallon glass containers holding 15 liters of test solution. Tests were started by introducing the test substance into the vessels containing dilution water, thoroughly mixing the solutions, then introducing the fish. Ten fish were placed into each test vessel. Fish loading in the test was 0.72 g/l. Observations for deaths and abnormal behavioral effects were made at 24, 48 and 96 hours.

Results

Nominal concentrations (mg/l):	0 (control), 1.0, 1.8, 3.2, 5.6 and 10 mg/l
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
Element Value:	96-hour LC_{50}
Statistical Results:	96-hour LC_{50} = 4.22 mg/l
Result:	Additional results included the following: 24-hour LC_{50} = 4.22 mg/l 48-hour LC_{50} = 4.22 mg/l The 96-hour no effect concentration was 1.8 mg/l.
Remarks:	100% mortality occurred in the 5.6 and 10 mg/l treatments within the first 24 hours. No further mortality occurred. Behavioral observations made during the test indicated that rainbow trout exposed to 3.2 mg/l and higher became stressed and showed signs of dark discoloration.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study

References — Dean, W. P. 1977. The Acute Toxicity of Arquad 2HT-75, Dimethyldi (hydrogenated tallow) ammonium chloride 75% Active, 1633602, to the Bluegill *Sunfish Lepomis machrochirus Rafinesque* and Rainbow *Trout Salmo gairdneri Richardson*. Study number 398-001. International Research and Development Corporation.

Other Available Reports — This report was also summarized for bluegill sunfish.

Other

Last Changed:	December 13, 2001
Order number for sorting:	17s trout
Remarks:	

4.1 Acute/Prolonged Toxicity to Fish

Test Substance

Identity:	Arquad 2HT-75 (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	OECD Guidelines for Testing of Chemicals, Guideline No. 203
Type:	Static acute
GLP:	Yes
Year:	1987
Species/Strain/Supplier:	Rainbow trout/not stated/Forellenhof Fredesloh
Analytical Monitoring:	No
Exposure Period:	96 hours
Statistical Methods:	Graphical plot of percent mortality vs log concentration
Remarks:	The report described the acute toxicity of the test substance to rainbow trout in a static exposure system. Rainbow trout were purchased and held in the laboratory during an adaptation period. During the first 12 days in holding, 7% mortality in the batch of fish occurred. Adaptation was continued for an additional five days with 0.5% mortality during that time. The fish were considered acceptable for testing at that time. During the adaptation period, fish were held in aerated dechlorinated city water under a 12 hour photoperiod. During testing, reconstituted water was used as dilution water. Hardness was not reported. In preparation for the start of the test, test vessels were filled with 10 l of reconstituted water and aerated for four days. After that period, water temperature, dissolved oxygen and pH were checked. Test substance was weighed and dispersed into a 2-liter beaker and stirred for 2 hours using a magnetic stirrer. Immediately afterward, the mixture was transferred from the beaker into the test vessel, and fish were distributed to each vessel. Each treatment consisted of two replicate vessels each holding five fish. Observations of mortality were made at 1, 24, 48, 72 and 96 hours. Temperature ranged from 14.3 to 14.8°C, dissolved oxygen ranged from 10.0 to 10.3 mg/l and pH remained at 8.1.

Results

Nominal concentrations (mg/l):	0 (control), 0.7, 1.2, 2.0, 3.5, 6.0, and 10 mg/l
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
Element Value:	96-hour LC_{50} = 3.4 mg/l
Statistical Results:	96-hour LC_{50} = 3.4 mg/l
Result:	In addition to the 96-hour LC_{50} value, the following information was included: LC_0 = 1.2 mg/l LC_{100} = 10.0 mg/l
Remarks:	100% mortality occurred within one hour at 10 mg/l. 70% mortality occurred by the end of the test at 6.0 mg/l. Zero mortality occurred at 3.5 mg/l, while 40% mortality occurred at 2.0 mg/l. No mortality occurred in the lower concentrations or control group.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; guideline study (OECD)

References

Dommröse, A. M. 1987. Investigation of the Lethal Effects of the Test Sample Arquad 2 HT-75 to the Rainbow Trout (OECD 203). NATEC Institute, Hamburg, Germany.

Other Available Reports

Other

Last Changed:	September 15, 2000
Order number for sorting:	17t
Remarks:	

4.1 Acute/Prolonged Toxicity to Fish

Test Substance

Identity:	Dihydrogenatedtallow dimethyl ammonium chloride (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Not stated
Type:	Acute
GLP:	Not stated
Year:	1974 - 1991
Species/Strain/Supplier:	Trout, medaka, fathead minnow, zebra fish, bluegill
Analytical Monitoring:	Not stated
Exposure Period:	96 hours
Statistical Methods:	Not stated
Remarks:	Twelve tests of 96-hour duration were reported in this review article. These tests used various types of exposure systems including those using laboratory-prepared water, lake water, and river water.

Results

Nominal concentrations (mg/l):	Not stated
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
Element Value:	

Species	Test duration (hours)	EC50 or LC50 (mg/l)	Reference
Salmo gairdneri	96	2.6	Akzo. 1987
	96	1.7	Kao Corp. 1990
Gasterosteus aculeatus	96	3.5	Roghair, et al. 1991
Oryzias latipes	96	5.2	Roghair, et al. 1991
Pimephales promelas	96	0.29 – 0.558	Versteeg. 1989
Lepomis macrochirus	96	0.62 – 2.17	Procter & Gamble. 1974 – 1986; Kappeler. 1982
	96	10.1 – 14.0	Procter & Gamble. 1974 – 1986; Kappeler. 1982
	96	0.56 – 3.2	Procter & Gamble. 1974 – 1986
	96	0.64	Procter & Gamble. 1974 – 1986
	96	14	Procter & Gamble. 1974 – 1986
	96	13	Procter & Gamble. 1974 – 1986
	96	7.7	Procter & Gamble. 1974 – 1986

Statistical Results: The EC_{50} or LC_{50} (not specified) ranged from 0.29 – 14 mg/l
Result: See table in Element Value above
Remarks: The variations in toxicity endpoints was reported to be due to differences in bioavailability of the test substance in various test systems.

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 2D
Remarks: Reliable with restrictions, information provided in an ECETOC technical report.

References

European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). 1993. DHTDMAC: Aquatic and Terrestrial Hazard Assessment. CAS RN 61789-80-8. Technical Report number 53, ISSN-0773-8072-53. ECETOC, Brussels, Belgium.

Akzo. 1987. Acute Toxicity of Arquad 2GT-75 to Rainbow Trout. Report number 86 9835/3. Akzo Chemicals International, BV, Amersfoort, The Netherlands.

Kao Corp. 1990. Acute Toxicity of DHTDMAC to Daphnia and Rainbow Trout. Report AT390/004 and AT 390/005. Kao Corporation SA, Puig dels Tudons, 10:08210, Barbera de Valles, Barcelona, Spain.

Kappeler, T. U. 1982. Die Aquatische Toxicität von DSDMAC und Ihre Ökologische Beduetung. Tenside Deterg. 19:169 – 176.

Procter & Gamble. 1974 – 1986. As Supplied to the ECETOC Task Force on DHTDMAC 1992. Data Available on Request from Procter & Gamble European Technical Centre, Professional and Regulatory Services, Brussels, Belgium.

Roghair, C. J., A. Buijze and H. N. P. Schoon. 1991. Maximum Permissible Level of the Cationic Surfactant DTDMAC for Aquatic Ecosystems. Report of the Dutch National Institute of Public Health and Environmental Protection. Report number 719102007.

Versteeg. 1989. Toxicity of Ditallowdimethylammonium chloride to Aquatic Organisms. Procter & Gamble Internal Notebook ZE 1340.

Other Available Reports

Other

Last Changed: December 13, 2001
Order number for Sorting: 20c
Remarks:

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Test Substance

Identity:	Arquad 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	86.0 %
Remarks:	

Method

Method/Guideline followed:	OECD Guidelines for Testing of Chemicals, Fish, Acute Toxicity Test, Procedure 203, adopted 4 April 1984
Type:	Semistatic
GLP:	Yes
Year:	1990
Species/Strain/Supplier:	Rainbow trout supplied by Hauxton Fisheries Services, Cambridge
Analytical monitoring:	Yes
Exposure period:	96 hours
Statistical methods:	Median lethal concentrations calculated using the computer program of Stephan et. al. (A computer program for calculating an LC_{50}. US Environmental Protection Agency); because measured concentrations were not all within 20% of their respective nominal values. LC_{50} values were calculated using means of measured concentrations.
Remarks:	Based on the results of a range-finding study, groups of ten juvenile rainbow trout/group were exposed to the test substance at nominal concentrations of 2.5, 5.0, 10.0, 20.0, 40.0 and 80.0 mg/l for 96 hours under static conditions. A control group was treated with dilution water alone. Fish were transferred to vessels containing freshly prepared test or control media at 48 hours. The mean wet weight of the fish, based on a sample of ten fish taken at random from the holding tank was 1.0 g. The mean fork length of these fish was 4.25 cm. The dilution water was treated tap water. The test was conducted at 13.7 ± 0.6 ºC in dilution water of hardness of 206 – 220 mg/l as $CaCO_3$ and pH 7.7 – 8.4. Test dilutions were prepared individually from an aqueous stock dispersion (nominally 1000 mg/l), which had been treated by ultrasound for 30 minutes. The test vessels were all-glass aquaria with a total capacity of 15 liters. Aeration of the contents of each vessel was achieved using a Pasteur pipette connected to an oil-free supply of compressed air. All glassware was conditioned to the test substance for approximately 48 hours before use. Observations of fish were made frequently during the initial four hours of test and thereafter at 24-hour intervals. Concentrations of the

test substance were measured in mid-vessel samples at each exposure concentration during the test.

Results

Nominal concentrations (mg/l): 2.5, 5.0, 10.0, 20.0, 40.0 and 80.0 mg/l
Measured concentrations (mg/l): 2.29, 7.72, 12.5, 20.1, 59.4 and 110.8 mg/l (by HPLC)
Unit: mg/l
LC_{50} (24-hour, measured): = 19.2 (95% Confidence Limits = 13.8 and 26.9 mg/l)
LC_{50} (48-hour, measured): ≈ 15.1
LC_{50} (72-hour, measured): ≈ 15.1
LC_{50} (96-hour, measured): ≈ 14.5
Statistical results: Described above
Remarks: The highest nominal concentration at which no mortality occurred and lowest at which there was 100% mortality after 96 hours were 5.0 and 20.0 mg/l, respectively. Mortality was not progressive during the test; the majority of the deaths occurred within the first 24 hours. No adverse effects were observed in test dilutions containing the test substance at nominal concentrations of 2.5 and 5.0 mg/l. The no observed effect concentration was considered to be 5.0 mg/l. Cumulative mortalities were as follows:

Dose level (mg/l)	**Minutes**	**Hours**					
	15	**2**	**4**	**24**	**48**	**72**	**96**
0	0/10	0/10	0/10	0/10	0/10	0/10	0/10
2.5	0/10	0/10	0/10	0/10	0/10	0/10	0/10
5.0	0/10	0/10	0/10	0/10	0/10	0/10	0/10
10.0	0/10	0/10	0/10	1/10	1/10	1/10	2/10
20.0	0/10	0/10	0/10	8/10	10/10	10/10	10/10
40.0	0/10	1/10	7/10	10/10	10/10	10/10	10/10
80.0	0/10	9/10	10/10	10/10	10/10	10/10	10/10

At all concentrations, test preparations were white, hazy dispersions with particulate material present on their surfaces. At 40 and 80 mg/l, the opacity of the media made it difficult to observe the fish at the start of the test. The appearance of these test dilutions did not change during the test.

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; Guideline study.

References

Jenkins, C. A. 1990. Arquad 3.16: Acute Toxicity to Rainbow Trout. Report number 90/AKL011/0347. Life Science Research Limited, Suffolk, UK.

Other

Last changed:	May 14, 2001
Order number for sorting:	33
Remarks:	

4.2 Acute Toxicity to Aquatic Invertebrates

Test Substance

Identity:	Dodecyl trimethyl ammonium chloride (C_{12}TMAC); (CAS RN 112-00-5)
Purity:	35%
Remarks:	

Method

Method/guideline followed:	U. S. EPA 1975. Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. Committee on Methods for Toxicity Tests with Aquatic Organisms. EPA-660/3-75-009.
Type:	Acute static
GLP:	Not stated
Year:	1983-1984
Species/Strain/Supplier:	*Ceriodaphnia sp.*/Not stated/Not stated
Analytical Monitoring:	Not stated
Exposure Period:	48 hours
Statistical methods:	Mortality data were analyzed by probit analysis to calculate the LC_{50} values and associated 95% confidence intervals. Survival was analyzed by chi-square techniques.
Remarks:	Water from Acton Lake was used for this test. *Ceriodaphnia sp.* were acclimated to the test conditions for at least two generations before use. *Ceriodaphnia sp.* were fed a diet of baker's yeast. For each test concentration, five neonate *Ceriodaphnia sp.* were placed in 30 ml of test solution in a 50 ml beaker. Three beakers were used per concentration per test. Test solutions were prepared by adding the test substance from a stock solution, prepared in deionized water (without the use of a solvent), to the test water. No aeration was used during the study. Mortality was recorded daily. The pH, and dissolved oxygen content were determined at the beginning and end of the test for one beaker in the control and lowest, middle and highest test concentrations. The LC_{50} value was based on nominal concentrations of the test substance.

Results

Nominal concentrations (mg/l):	Not stated
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
LC_{50} (48 hour):	= 0.39 mg/l (95% confidence intervals of 0.35 – 0.43 mg/l)
NOEC (48 hour):	Not stated

Remarks: The physiochemical characteristics of the Acton Lake water were: Total hardness = 197 mg/l as $CaCO_3$; pH = 7.3; total suspended solids = 9.9 mg/l; and dissolved oxygen = 9.4 mg/l.

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 1B

Remarks: Reliable without restriction; comparable to guideline study.

References

Taylor, M. J. 1984. Cooperative Sensitivity of *Ceriodaphnia Sp.* and *Daphnia Magna* to Select Surfactants. Procter & Gamble Co., Cincinnati, OH, US. Unpublished report (Notebook: ZE-1154 and ME-1082).

Other Available Reports

Other

Last changed: November 16, 2001

Order number for sorting: 110

Remarks:

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Dodecyl trimethyl ammonium chloride (C_{12}TMAC); (CAS RN 112-00-5)
Purity:	35%
Remarks:	

Method

Method/guideline followed:	Not stated
Type:	Acute
GLP:	Not stated
Year:	1983-1984
Species/Strain/Supplier:	*Ceriodaphnia sp.*/Not stated/Not stated
Analytical Monitoring:	Not stated
Exposure Period:	48 hours
Statistical methods:	Mortality data were analyzed by probit analysis to calculate the LC_{50} values. Survival was analyzed by chi-square techniques. Reproduction was analyzed by ANOVA.
Remarks:	Ohio River water was collected weekly from the shoreline at the Public Landing in downtown Cincinnati. Ohio River water physiochemical characteristics: Total hardness = 156 mg/l as $CaCO_3$; pH = 7.0 to 7.7; total suspended solids = 98 mg/l; and dissolved oxygen = 10.7. *Ceriodaphnia sp.* were acclimated to the test conditions for at least two generations before use. The LC_{50} value was based on nominal concentrations.

Results

Nominal concentrations (mg/l):	0, 0.05, 0.10, 0.20, 0.30, 0.40 and 0.60 mg/l
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
LC_{50} (48 hour):	= 0.345 mg/l (with 95% confidence intervals of 0.266 – 0.477 mg/l)
NOEC (48 hour):	0.20 mg/l
Result:	Concentrations of 0.40 mg/l and higher of the test substance resulted in 100% mortality. Mortality also was increased (40%) at 0.30 mg/l.
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 1B

Remarks: Reliable without restriction; comparable to guideline study.

References

Taylor, M. J. 1984. Cooperative Sensitivity of *Ceriodaphnia Sp.* and *Daphnia Magna* to Test Chemicals. Procter & Gamble Co., Cincinnati, OH, US. Unpublished report (Notebook: 25-1154, Vol., 2).

Other Available Reports

Other

Last Changed: November 16, 2001

Order Number for Sorting: 106

Remarks:

4.2 Acute Toxicity to Aquatic Invertebrates

Test Substance

Identity:	Monotallowtrimethyl ammonium chloride (CAS RN 8030-78-2; quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	non-radiolabeled: 48.4%
Remarks:	Stock solutions were prepared using non-radiolabeled test substance and radiolabeled ^{14}C-Alkyl Stearyl trimethyl ammonium chloride (^{14}C-STAC) in isopropanol. Purity of ^{14}C-STAC was 98%

Method

Method/guideline followed:	Not stated
Type:	Acute
GLP:	Not stated
Year:	1980-1981
Species/Strain/Supplier:	*Daphnia magna* /Not stated/Not stated
Analytical Monitoring:	Yes
Exposure Period:	48 hours
Statistical Methods:	The 48-hour LC_{50} values were determined by probit analysis based on the geometric mean of the 0-, 24- and 48-hour concentrations to reflect overall exposure concentrations.
Remarks:	Three water types were utilized in this test: laboratory blended water (total hardness ~150 mg/l), Southwest well water (total hardness ~350 mg/l) and river water (total hardness ~300-350 mg/l). The river water, exemplifying a natural surface water that received sewage effluent, was collected from the White River (Indiana) and transported for cold storage (~4°C). Acute toxicity tests of 48-hour duration were conducted in each water type employing seven concentrations of test substance plus control and an isopropanol (IPA) control. The tests were repeated to ensure reproducibility. The same procedures were utilized in the repeat tests with the exception of testing a more recently collected batch of White River water. There was no renewal of test waters throughout the 48-hour test period. Mortality was recorded daily and water chemistry measurements were taken at the beginning and conclusion of the test period for control waters only. Each test material concentration was verified by radiochemical counting of triplicate 10 ml samples collected from the fresh stock solution (0 hour) and from a randomly selected beaker after 24 and 48 hours.

Results

Nominal concentrations (µg/l): Blended water and Southwest well water: 11.5, 15.5, 21.0, 28.0, 37.0, 49.0 and 65.0 µg/l
River water: 115, 155, 210, 280, 370, 490 and 650 µg/l

Measured concentrations (µg/l): Values in the table represent the geometric mean of the 0-, 24- and 48-hour concentration analyses:

Nominal concentration (µg/l)	Blended water I : R* (µg/l)	Southwest well water I : R* (µg/l)
11.5	3.3 : 4.4	2.8 : 3.9
15.5	5.3 : 6.0	3.9 : 6.1
21.0	9.0 : 8.9	5.9 : 8.6
28.0	10.6 : 12.1	8.9 : 11.8
37.0	15.7 : 14.5	14.3 : 14.4
49.0	17.4 : 22.9	19.6 : 24.3
65.0	29.5 : --	29.2 : 37.9

* I : R = value for initial test : value for repeat test
-- = concentration level not repeated

Nominal concentration (µg/l)	River water (initial test) (µg/l)
115	35.0
155	39.0
210	57.7
280	87.5
370	129.6
490	162.1
650	214.2

Unit: µg/l

LC_{50} (48 hour): = 17.5 µg/l in Southwest well water (the 48-hour LC_{50} values in the initial and repeat tests were 19.8 and 15.3 µg/l, respectively).
= 12.6 µg/l in blended water (the 48-hour LC_{50} values in the initial and repeat tests were 16.3 and 8.8 µg/l, respectively).
= 98.9 µg/l in river water (initial test result only)

NOEC (48 hour): Not stated

Result:

Mortality at 48 hours (initial N = 20)		
Nominal concentration (µg/l)	**Blended water I : R***	**Southwest well water I : R***
Control	0 : 0	1 : 1
IPA control	0 : 2	0 : 0
11.5	1 : 0	0 : 4
15.5	1 : 2	0 : 2
21.0	0 : 13	0 : 1
28.0	0 : 16	0 : 9
37.0	8 : 20	7 : 8
49.0	13 : 20	10 : 20
65.0	20 : --	15 : 20

* I : R = number dead in initial test : number dead in repeat test
-- = concentration level not repeated

Mortality at 48 hours (initial N = 20)	
Nominal concentration (µg/l)	**River water (initial test)**
Control	2
IPA control	0
115	0
155	0
210	3
280	15
370	20
490	20
650	20

Remarks:

Distribution and removal studies were conducted prior to the acute toxicity tests. Because of the very rapid removal of the test substance from the water column, the geometric mean of the 0, 24 and 48-hour concentrations was considered to be the overall exposure concentration in the acute toxicity tests.
The acute test in river water was repeated using the same concentration range as the initial test. Mortality in this repeat test was 100% at the next to lowest concentration; therefore, the test was repeated a second time utilizing a more recently collected batch of river water and adjusting the concentration range to bracket an LC_{50} value estimated from the previous test. In this test, no significant mortality occurred at any concentration.

Conclusions In the initial acute toxicity tests, little difference existed between LC_{50} values for blended and well waters. The river water LC_{50}, however, was 5 to 11 times higher, possibly related to the presence of solids causing test substance adsorption and reduced bioavailability. An additional factor may have been that the river water contained endogenous nutritional sources perhaps enhancing daphnid resistance to the effects of the test substance.

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 1B

Remarks: Reliable without restriction; comparable to guideline study.

References

Valentine, L. C. and W. E. Bishop. 1992. Effects of MTTMAC on the Survival and Reproduction of *Daphnia Magna* in Laboratory Waters and a Natural Surface Water. Procter & Gamble Co., Cincinnati, OH, USA. Unpublished report (Notebook: ME-5004, ME-5007 and ZE-1111).

Other Available Reports

Other

Last Changed: November 16, 2001

Order Number for Sorting: 301

Remarks:

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (DTDMAC); (CAS RN 68783-78-8)
Purity:	71.4%
Remarks:	

Method

Method/guideline followed:	U. S. EPA 1975. Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. Committee on Methods for Toxicity Tests with Aquatic Organisms. EPA-660/3-75-009.
Type:	Acute static
GLP:	Not stated
Year:	1983-1984
Species/Strain/Supplier:	*Ceriodaphnia sp.*/Not stated/Not stated
Analytical Monitoring:	Not stated
Exposure Period:	48 hours
Statistical methods:	Mortality data were analyzed by probit analysis to calculate the LC_{50} values and associated 95% confidence intervals. Survival was analyzed by chi-square techniques. Reproduction was analyzed by ANOVA.
Remarks:	Three acute toxicity tests were performed with *Ceriodaphnia s.* in the following conditions: 1) test conducted in Ohio River water and the *Ceriodaphnia sp.* fed a diet consisting of a mixture of algae, trout chow and alfalfa; 2) test conducted in Ohio River water and the *Ceriodaphnia sp.* fed a diet of baker's yeast; and 3) test conducted in Acton Lake water and *Ceriodaphnia sp.* fed a diet of baker's yeast. *Ceriodaphnia sp.* were acclimated to the test conditions for at least two generations before use. For each test concentration, five neonate *Ceriodaphnia sp.* were placed in 30 ml of test solution in a 50 ml beaker. Three beakers were used per concentration per test. Test solutions were prepared by adding the test substance from a stock solution, prepared in deionized water, to the test water. The test substance stock solution was prepared by first dissolving the test substance in isopropyl alcohol (which did not exceed 0.01% in the test solutions). No aeration was used during the study. Mortality was recorded daily. The pH, and dissolved oxygen content were determined at the beginning and end of the test for one beaker in the control and lowest, middle and highest test concentrations. The LC_{50} value was based on nominal concentrations of the test substance.

Results

Nominal concentrations (mg/l): Not stated
Measured concentrations (mg/l): Not stated
Unit: mg/l
LC_{50} (48 hour):

Water	Diet	48-hour LC_{50} (95% confidence limit)
Ohio River	Algae-trout chow	1.23 mg/l (0.60 – 1.74 mg/l)
Ohio River	Baker's yeast	0.54 mg/l (0.22 – 0.80 mg/l)
Acton Lake	Baker's yeast	1.23 mg/l (0.96 – 1.53 mg/l)

NOEC (48 hour): Not stated
Remarks: The physiochemical characteristics of the Acton Lake water were: Total hardness = 197 mg/l as $CaCO_3$; pH = 7.3; total suspended solids = 9.9 mg/l; and dissolved oxygen = 9.4 mg/l. The physiochemical characteristics of the Ohio River water were: Total hardness = 110 mg/l as $CaCO_3$; pH = 7.4; total suspended solids = 87 mg/l; and dissolved oxygen = 9.7 mg/l. The 48-hour LC_{50} determined for *Ceriodaphnia sp.* fed baker's yeast and exposed to test concentrations in Ohio River water was significantly different from the LC_{50} in the other two groups tested.

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 1B
Remarks: Reliable without restriction; comparable to guideline study.

References

Taylor, M. J. 1984. Cooperative Sensitivity of *Ceriodaphnia Sp.* and *Daphnia Magna* to Select Surfactants. Procter & Gamble Co., Cincinnati, OH, US. Unpublished report (Notebook: ZE-1154 and ME-1082).

Other Available Reports

Other

Last changed: November 15, 2001
Order number for sorting: 603
Remarks:

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (DTDMAC); (CAS RN 68783-78-8)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	U. S. EPA 1975. Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. Committee on Methods for Toxicity Tests with Aquatic Organisms. EPA-660/3-75-009.
Type:	Acute static
GLP:	Not stated
Year:	1983
Species/Strain/Supplier:	Eastern oyster embryos/(*Crassostrea verginica*); Mysid shrimp (*Mysidopsis bahia*); Pink shrimp (*Penaeus duorarum*); and Blue crabs (*Callinectes sapidus*). All species were obtained from the Big Lagoon near Pensacola, Florida. *Daphnia magna*/obtained from the testing laboratory.
Analytical Monitoring:	Yes
Exposure Period:	48 hours for the oyster embryos and *Daphnia magna*; and 96 hours for both species of shrimp and the blue crab.
Statistical Methods:	Mortality data were analyzed by probit analysis or other accepted statistical procedures.
Remarks:	Procedures for the 48-hour static test for the oyster are as follows: Oyster embryos were obtained by induced spawning of sexually mature individuals. Approximately 50,000 embryos were exposed to each of the five test substance concentrations and the control in 1-liter glass aquaria containing 900 ml filtered (5µm) seawater. The test substance concentrations and the controls were tested in triplicate. The reduction of the number of normal embryos that developed to the fully-shelled, straight-hinged veliger stage was monitored during the 48-hour exposure. The LC_{50} values were based on nominal concentrations. Procedures for the 96-hour static test for the shrimp and crab are as follows: The tests were conducted in 19-liter glass aquaria containing 15 liters of filtered, natural seawater. Salinity ranged from 16 to 26‰ during testing, and the water temperature was maintained at 20 ± 1°C for all tests. Ten sheepshead minnows (15-20 mm) were exposed to each of five test concentrations and the control.

Mortality was recorded daily. The LC_{50} values were based on nominal concentrations.
Procedures for the 48-hour static test for the *Daphnia magna* are as follows: Daphnids used in this test were < 24 hours old. Tests were conducted in 250 ml glass beakers containing either 150 or 200 ml test solution. The test vessels were maintained at 19 to 22°C and were not aerated during testing. Mortality of the daphnids in each chamber were recorded daily. Test waters utilized were reconstituted water (two tests) and well water. Chemical and physical qualities of the reconstituted water was as follows: pH 6.5 – 7.3; total harness 131 – 163 mg/l $CaCo_3$; suspended solids 0 mg/l; chlorinated insecticides < 0.005 µg/l; and organophosphates <0.01 µg/l. Chemical and physical qualities of the well water was as follows: pH 7.1 – 7.9; total harness 315 – 348 mg/l $CaCo_3$; suspended solids 0 mg/l; chlorinated insecticides < 0.005 µg/l; and organophosphates <0.01 µg/l. The five test substance concentrations, the control and where appropriate the solvent control were done in triplicate.

This publication presents data for a number of species and does not specify concentrations used for assay. The values are included in the dataset since they provide information consistent with the data for the category.

Results

Nominal concentrations (mg/l): Not stated
Measured concentrations (mg/l): Not stated
Unit: mg/l
LC_{50} (48 hour):

Species	Water	48 hour LC_{50} (95% confidence limit))
Eastern oyster embryos	Filtered seawater	2.0 mg/l (1.2 – 3.4 mg/l)
Daphnia magna	Reconstituted	0.19 to 0.48 mg/l
Daphnia magna	Well	1.06 mg/l (0.91 – 1.25 mg/l)

LC$_{50}$ (96 hour):

Species	Water	96 hour LC$_{50}$ (95% confidence limit))
Mysid shrimp	Natural seawater	0.22 mg/l (0.17 – 0.30 mg/l)
Pink shrimp	Natural seawater	36 mg/l
Blue crabs	Natural seawater	> 50 mg/l

NOEC (48 hour): Not stated
Remarks:

Conclusions The data are useful in support of the overall category. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality
Reliability (Klimisch): 2B
Remarks: Reliable with restriction; basic data given

References Lewis, M. A. and V. T. Wee. 1983. Aquatic Safety Assessment for Cationic Surfactants. Microbiological Associates, Bethesda, MD, USA. Unpublished report (No. T1806.501).

Other
Last changed: November 16, 2001
Order number for sorting: 604
Remarks:

4.2 Toxicity to Aquatic Invertebrates

Test Substance

Identity: Dihydrogenatedtallow dimethyl ammonium chloride (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)

Purity: Not stated

Remarks:

Method

Method/guideline followed: Not stated

Type: Acute

GLP: Not stated

Year: Various studies reported

Species/Strain/Supplier: *Daphnia magna*/Not stated/Not stated

Analytical Monitoring: Not stated

Exposure Period: 48 hours

Statistical Methods: Not stated

Remarks: Twelve tests of 48-hour duration were reported in this review article. These tests used various types of exposure systems including those using laboratory-prepared water, well water and river water.

Results

Nominal concentrations (mg/l): Not stated

Measured concentrations (mg/l): Not stated

Unit: mg/l

EC_{50} (48 hour):

Species	Test Duration (hrs)	EC_{50} or LC_{50} (mg/l)	Reference
D. magna	48	0.16 – 1.06	Kappeler. 1982
	48	2.6 – 3.1	Kappeler. 1982
	24	0.9	Fina. 1989
	48	0.24	Kao Corp. 1990
	48	0.35	Berol Nobel. 1990b
	48	0.1	Unilever. 1990, 1991
	48	0.48	Atochem. 1990b
	96	0.48	Procter & Gamble. 1974 – 1986
	48	0.065	Procter & Gamble. 1974 – 1986
	48	0.28	Procter & Gamble. 1974 – 1986
	48	0.19	Procter & Gamble. 1974 – 1986
	48	1.06	Procter & Gamble. 1974 – 1986
	48	2.1	Procter & Gamble. 1974 – 1986
	48	3.6	Procter & Gamble. 1974 – 1986

LC_{50} (48 hour):	See above
NOEC (48 hour):	Not stated
Result:	The EC_{50} or LC_{50} (not specified) ranged from 0.065 to 3.6 mg/l.
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions, information provided in an ECETOC technical report.

References

European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). 1993. DHTDMAC: Aquatic and Terrestrial Hazard Assessment. CAS RN 61789-80-8. Technical Report number 53, ISSN-0773-8072-53. ECETOC, Brussels, Belgium.

Kappeler, T. U. 1982. Die Aquatische Toxicität von DSDMAC und Ihre Ökologische Bedeutung. Tenside Deterg.. 19:169 – 176.

Fina. 1989. Acute Toxicity of Dihydrogenated tallow dimethyl ammonium chloride to *Daphina magna* (DHTDMAC). Report B.7113. Sanofi Research, Montpellier, France.

Kao Corp. 1990. Acute Toxicity of DHTDMAC to Daphnia and Rainbow Trout. Report AT309/004 and AT309/005. Kao Corporation SA, Puig dels Tudons, 10:08210, Barbera de Valles, Barcelona, Spain.

Berol Nobel. 1990. Acute Toxicity of DHTDMAC to *Daphnia magna*. Report 116/52. Berol Nobel 4B, Nacka, Sweden.

Unilever. 1990 – 1991. Ecotoxicity Data for Surfactants. Data as supplied to the AIS/CESIO Task Force. Port Sunlight Laboratory, Merseyside, UK

Atochem. 1990. Acute Toxicity of Noramium M2SH to *Daphnia magna*. Report 1/10/90. Atochem centre d'appliation de Levallois, France.

Procter & Gamble. 1974 – 1986. As Supplied to the ECETOC Task Force on DHTDMAC 1992. Data Available on Request from Procter & Gamble European Technical Centre, Professional and Regulatory Services, Brussels, Belgium.

Other Available Reports

Other

Last Changed:	December 13, 2001
Order number for Sorting:	20c
Remarks:	

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Arquad 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	86.0 %
Remarks:	

Method

Method/Guideline followed:	OECD Guidelines for Testing of Chemicals, *Daphnia* sp., Acute Immobilization Test and Reproduction Test, Part 1, Procedure 202, adopted 4 April 1984
Test type:	Static
GLP:	Yes
Year:	1990
Analytical procedures:	Yes
Species/Strain:	*Daphnia magna*/strain from University of Sheffield and originated form the National Institute for Applied Chemical Research, France
Test details:	Static
Statistical methods:	Median effect concentrations calculated using the computer program of Stephan et. al. (A computer program for calculating an LC_{50}. US Environmental Protection Agency); because measured concentrations were not all within 20% of their respective nominal values, EC_{50} values were calculated using means of measured concentrations
Remarks:	Based on the results of a range-finding test, groups of 20 *Daphnia* were exposed to the test substance at nominal concentrations of 0.1, 0.18, 0.32, 0.56 and 1.0 mg/l in a 48-hour static renewal acute toxicity test. Two control groups were included in the test; one was exposed to dilution water alone, and the other to dilution water containing acetone at a concentration of 0.1 ml/l. Duplicate vessels were employed at each level. All glassware used during the test was conditioned to the test substance for approximately 48 hours before use. *Daphnia* were maintained in parthenogenetic culture at the Aquatic Studies Laboratories of Life Science Research since receipt. Observations of the *Daphnia* were made 24 and 48 hours after the start of the test. The appearance of the test substance in water was noted during the test. Temperature, pH and concentration of dissolved oxygen of the control and test media, measured at the start and end of the tests, ranged from 18.4 – 19.9 ºC, 8.18 – 8.41, 96 – 100 mg/l, respectively. Total hardness as mg/l $CaCO_3$ and alkalinity as mg/l $CaCO_3$ ranged from 214 – 224 and 138 – 145, respectively.

The sodium:potassium ratio and calcium:magnesium ratio ranged from 4.9:1 and 21.8:1, respectively.

Results

Nominal concentrations (mg/l): 0, 0.1, 0.18, 0.32, 0.56 and 1.0 mg/l
Measured concentrations (mg/l): at 48 hours: 0, 0.92, 0.157, 0.281, 0.512 and 0.802 mg/l
Unit: mg/l
EC_{50} (24-hour, measured): 0.21 (95% Confidence Limits = 0.17 and 0.26 mg/l)
EC_{50} (48-hour, measured): 0.11 (95% Confidence Limits = 0.09 and 0.12 mg/l)
Remarks: At the start of the test, mean measured concentrations of the test substance were ranging from 121 to 191% of their nominal values. After 48 hours, exposure levels dropped to between 46 to 76% of the starting concentrations. The observed variation in measured concentration was thought to reflect the presence of undissolved test material in the samples. All test concentrations were clear and colorless and remained unchanged during the test. The lowest nominal exposure concentration used in the test (0.1 mg/l) resulted in 30% immobility after 48 hours; the lowest concentration at which there was 100% immobility was 0.32 mg/l. Following is a summary of the cumulative immobility:

Nominal Test Concentration (mg/l)	Cumulative Immobility	
	24 hours	**48 hours**
0.0	0/20	0/20
0.0 (acetone)	0/20	1/20
0.1	2/20	6/20
0.18	11/20	18/20
0.32	7/20	20/20
0.56	19/20	20/20
1.0	20/20	20/20

At 0.18, 0.32 and 0.56 mg/l, some of the immobile *Daphnia* were floating on the surface of the test dilutions. The pattern of immobility was dose-related.

Conclusions

Remarks: The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1A
Remarks: Reliable without restriction; guideline study.

References Jenkins, C. A. 1990. Arquad 3.16: acute toxicity to *Daphnia magna*. Report number 90/AKL012/0348. Life Science Research Limited, Suffolk, UK.

Other

Last changed:	May 14, 2001
Order number for sorting:	32
Remarks:	

4.3 Toxicity to Aquatic Plants (Algae)

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (DTDMAC); (CAS RN 68783-78-8)
Purity:	97.7%
Remarks:	The test was conducted with pure distearyl dimethyl ammonium chloride. The test substance was specially synthesized to ensure the absence of MTTMAC

Method

Method/guideline followed:	Horning, W. B. and C. I. Weber. 1985. Short-term Methods for Estimating the Chronic Toxicity of Effluents and Receiving Waters to Freshwater Organisms. EPA-600/4-85-014. U. S. EPA, Cincinnati, Ohio.
Type:	Static
GLP:	Yes
Year:	1987-1988
Species/Strain/Supplier:	Green algae (*Selenastrum capricornutum*)/Not stated
Element Basis:	10^6 cells
Analytical Monitoring:	Yes
Exposure Period:	Four days
Statistical methods:	Probit analysis was used to calculate the lethal concentrations. For nonquantal data, effective concentrations causing a 20 percent decrease in the appropriate population level parameter and the associated 95% confidence intervals were calculated by nonlinear multiple regression analysis on SAS.
Remarks:	Acidic methanol was used as a carrier solvent in the toxicity test due to the low water solubility of the test substance. A solvent control group was included with each toxicity test. Filtered Little Miami River water was used for all tests. Dissolved oxygen and pH were monitored in the control and highest test concentration having survivors. The algal toxicity test was initiated by placing 10^6 cells from a culture in logarithmic phase growth into 100 ml of the test solution. Test solutions were continually stirred (100 rpm) at 25°C with constant illumination of approximately 400 ft-c cool white fluorescent light. At 96 hours, the concentration of algal cells in the test solutions were determined manually with a hemocytometer. Toxicity was manifested as a decrease in cell numbers as compared to the controls.

Results

Nominal concentrations (mg/l): Not stated
Measured concentrations (mg/l): 0, 0.6, 10, 4.2, 9.9 and 16.4 mg/l
Unit: mg/l
Element value: EC_{50} (48-hours) = 1.53 mg/l (95% confidence limit of 1.01 – 2.30 mg/l)
EC_{50} (96 hours) = 1.12 mg/l (95% confidence limit of 0.756 – 1.67 mg/l)
The four day algistatic concentration, was > 16.4 mg/l
NOEC:
Satisfactory control response: Yes
Statistical results: See above.
Remarks: Algal populations exposed to solvent control concentrations of 32 and 125 µl/l had increased growth relative to the blank control algal populations. The concentrations of solvent used in the test substance exposure groups ranged from 3 to 125 µl/l. A dose-dependent decrease in algal growth was observed in the test substance exposure groups.

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 1B
Remarks: Reliable without restriction; comparable to guideline study.

References

Shorter, S. J. 1993. The Chronic Effects of DTDMAC on the Fathead Minnow (*Pimephales promelas*) Larval Survival and Growth. Procter & Gamble Co., Cincinnati, OH, USA. Unpublished report (Report No. E89-006).

Other

Last changed: November 15, 2001
Order number for sorting: 605
Remarks:

4.3 Toxicity to Aquatic Plants (Algae)

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (DTDMAC); (CAS RN 68783-78-8)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Payne A. G. And R. H. Hall. 1979. A method for measuring algal toxicity and its application to the safety assessment of new chemicals. In L. L. Marking and R. A. Kimerle, eds., *Aquatic Toxicology*, ASTM STP 667. American Society for Testing and Materials, Philadelphia, PA, pp. 171-180.
Type:	Chronic/subchronic
GLP:	Not stated
Year:	Not stated
Species/Strain/Supplier:	Green algae (*Selenastrum capricornutum*); Blue-green algae (*Microcystis aeruginosa*); Diatom (*Navicula seminulum*); and Marine flagellate (*Dunalliela tertiolecta*)
Element Basis:	Not stated
Analytical Monitoring:	Not stated
Exposure Period:	Five days
Statistical Methods:	Not stated
Remarks:	The culture procedures for the species followed the Algal Assay Procedure (AAP) Bottle Test and, where appropriate, the Marine Algal Assay Procedure (MAAP) Bottle Test. Before use, river water was either filtered through a 0.45 µm filter or autoclaved to remove indigenous algal species. A control and solvent control were included in all tests.

Results

Nominal concentrations (mg/l):	0, 0.01, 1.0, 10, 50 and 100 mg/l
Measured concentrations (mg/l):	Not stated
Unit:	mg/l

Element value:

Species	Dilution Water	Algistatic Concentration (95% confidence limit)	Algicidal Concentration (mg/l)
Selenastrum capricornutum	Distilled	0.23 mg/l (0.16 – 0.32)	--
	White River (autoclaved)	0.71 mg/l (0.44 – 1.15)	--
	Rapid River (autoclaved)	2.6 mg/l (0.5 – 5.3)	--
	Rapid River (filtered)	> 4.0 mg/l	--
Microcystis aeruginosa	Distilled	0.32 mg/l	--
	Whit River (autoclaved)	0.21 mg/l	--
Navicula seminulum	Distilled	> 0.5 mg/l ≤ 10.0 mg/l	> 0.5 mg/l ≤ 10.0 mg/l
Dunalliela tertiolecta	Seawater	> 0.5 mg/l ≤ 1.0 mg/l	>1.0 mg/l ≤ 10.0 mg/l

Satisfactory control response: Not stated
Statistical results: See Element Values above
Remarks: None

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 2B
Remarks: Reliable with restriction; basic data given.

References

Lewis, M. A. and V. T. Wee. 1983. Aquatic Safety Assessment for Cationic Surfactants. Microbiological Associates, Bethesda, MD, USA. Unpublished report (No. T1806.501).

Other

Last changed: November 15, 2001
Order number for sorting: 604
Remarks:

4.3 TOXICITY TO AQUATIC PLANTS (ALGAE)

Test Substance

Identity:	Dihydrogenatedtallow dimethyl ammonium chloride (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Not stated
Type:	Chronic/subchronic
GLP:	Not stated
Year:	Not stated
Species/Strain/Supplier:	*Scenedesmus pannonicus*, *Microcycstic aeruginosa*, *Selenastrum capricornutum*, *Navicula seminulum*, *Chlorella vulgaris*
Element Basis:	Not stated
Analytical Monitoring:	Not stated
Exposure Period:	Four to five days
Statistical Methods:	Not stated
Remarks:	Eighteen tests of 4 – 5 day duration were reported in this review article.

Results

Nominal concentrations (mg/l):	Not stated
Measured concentrations (mg/l):	Not stated
Unit:	mg/l

Element value:

Species	Test Method	NOEC (mg/l)	EC50 (mg/l)	References
Scenedesmus pannonicus	growth inhib. 96 h	0.58	1.8	Roghair, *et al.* 1991.
Microcystis aeruginosa	growth inhib. 96 h		0.05	Procter & Gamble. 1974 - 1986
Microcystis aeruginosa	growth inhib. 5 d	0.13		Procter & Gamble. 1974 - 1986
Microcystis aeruginosa	growth inhib. 5 d	0.075		Procter & Gamble. 1974 - 1986
Microcystis aeruginosa	growth inhib. 5 d	0.078		Procter & Gamble. 1974 - 1986
Selenastrum capriconutum	growth inhib. 96 h	0.12	0.21	Akzo. 1991a
Selenastrum capriconutum	growth inhib. 96 h	0.006	0.026	Akzo. 1991b
Selenastrum capriconutum	growth inhib. 96 h		0.06	Lewis. 1990
Selenastrum capriconutum	growth inhib. 96 h	20.3		Versteeg & Woltering. 1990
Selenastrum capriconutum	growth inhib. 96 h	10.7		Versteeg & Woltering. 1990
Selenastrum capriconutum	growth inhib. 5 d	0.075		Procter & Gamble. 1974 - 1986
Selenastrum capriconutum	growth inhib. 5 d	0.078		Procter & Gamble. 1974 - 1986
Selenastrum capriconutum	growth inhib. 5 d	0.25		Procter & Gamble. 1974 - 1986
Selenastrum capriconutum	growth inhib. 5 d	0.12		Procter & Gamble. 1974 - 1986
Selenastrum capriconutum	growth inhib. 5 d	0.062		Procter & Gamble. 1974 - 1986
Navicula seminulum	growth inhib. 5 d	0.05		Procter & Gamble. 1974 - 1986
Chlorella vulgaris	growth inhib. 96 h		0.4	Unilever. 1990 - 1991
Chlorella vulgaris	growth inhib. 96 h		0.27	Unilever. 1990 - 1991

Result: EC_{50} values ranged from 0.026 to 1.8 mg/l. No-observed-effect concentrations (NOECs) ranged from 0.006 to 0.58 mg/l.
Satisfactory control response: Not stated
Statistical results: See Result above
Remarks: The variations in toxicity endpoints was reported to be due to differences in bioavailability of the test substance in various test systems.

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 2D
Remarks: Reliable with restrictions, information provided in an ECETOC technical report.

References

European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). 1993. DHTDMAC: Aquatic and Terrestrial Hazard Assessment. CAS RN 61789-80-8. Technical Report number 53, ISSN-0773-8072-53. ECETOC, Brussels, Belgium.

Akzo. 1991a. Algal Growth Inhibition Test with DHTDMAC. Report R90/364. Chemicals International, BV, Amersfoort, The Netherlands.

Akzo. 1991b. Algal Growth Inhibition Test with Distearyl dimethyl ammonium chloride (DSDMAC). Report CRL F90096. Chemicals International, BV, Amersfoort, The Netherlands.

Lewis, M. A.. 1990. Chronic Toxicities of Surfactants and Detergent Builders to Algae: A Review and Risk Assessment. Ecotoxicology and Environmental Safety. 20:123.

Procter & Gamble. 1974 – 1986. As Supplied to the ECETOC Task Force on DHTDMAC 1992. Data Available on Request from Procter & Gamble European Technical Centre, Professional and Regulatory services, Brussels, Belgium.

Roghair, C. J., A. Buijze and H. N. P. Schoon. 1991. Maximum Permissible Level of the Cationic Surfactant DTDMAC for Aquatic Ecosystems. Report of the Dutch National Institute of Public Health and Environmental Protection. Report number 719102007.

Unilever. 1990 – 1991. Ecotoxicity Data for Surfactants. Data As Supplied to the AIS/CESIO Task Force. Port Sunlight Laboratory, Merseyside, UK.

Other Available Reports

Other

Last Changed: December 13, 2001
Order number for Sorting: 20c
Remarks:

4.3 Toxicity to Aquatic Plants (Algae)

Test Substance

Identity:	Arquad 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	70.8% (based on R3N content and 87.9% activity)
Remarks:	

Method

Method/guideline followed:	OECD, EEC and ISO Test Guidelines
Test type:	Static
GLP:	Yes
Year:	1994
Species/Strain/Source:	*Selenastrum capricornutum*
Element basis:	4.7 x 10^5 cells/ml in the control flask at the end of the test (96 hours)
Exposure period:	96 hours
Analytical monitoring:	Yes
Statistical methods:	Not stated
Remarks:	Based on the results of a range-finding test, *Selenastrum capricornutum* was exposed to the test substance at nominal concentrations of 0.035, 0.071, 0.142, 0.283 and 0.566 mg/l. The toxicity of the test substance to exponentially growing *Selenastrum capricornutum* was determined over an exposure period of 96 hours. The test was conducted in a mineral salts medium at temperatures ranging from 23.7 to 24.6 ºC in an illuminate orbital incubator. The pH in the test media varied from 8.2 to 9.1. Prior to use on the study, the test flasks were conditioned to the test substance by adding the test substance to the vessels using the same concentration range as used in the definitive test. The test was performed using six replicates of the control and three replicates at each concentration.

Results

Nominal concentrations (mg/l):	0.035, 0.071, 0.142, 0.283 and 0.566 mg/l
Measured concentrations (mg/l):	Concentrations were measured only from the lowest (0.035 mg/l), middle (0.142 mg/l) and highest (0.566 mg/l) concentrations. Results at 0 hours = 0.03, 0.14 and 0.51 mg/l, respectively. Results at 96 hours = 0.01, 0.03 and 0.38 mg/l, respectively.
Unit:	mg/l

Element Value:	E_bC_{50} (growth; 0 – 96-hour) = 0.113 mg/l (95% Confidence Limits = 0.106 – 0.121 mg/l) E_rC_{50} (growth rate; 0 – 96-hour) = 0.177 mg/l (95% Confidence Limits = 0.169 – 0.191 mg/l)
NOEC:	0.035 mg/l
LOEC:	0.071 mg/l
Satisfactory control response:	Described below
Statistical results:	Described above
Remarks:	The test was valid as shown by the E_bC_{50} and E_rC_{50} values of the reference compound, potassium dichromate (0.8 and 1.5 mg/l, respectively), the increase of the extinction of the control over 72 hours by a factor of 16 and by a maximum deviation of the pH of 0.9 units. Chemical analysis, using HPLC, of duplicate samples taken at the beginning of the test indicated that the exposure concentrations were substantially achieved (85 – 99% of the nominal values). The concentrations at the end of the test were strongly decreased (21 – 67% of the nominal values), probably due to adsorption of the test substance to the test flask walls.

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction, guideline study.

References

Kroon, A. G. M. and Geurts, M. G. J. 1994. Toxicity of Arquad 3.16 to the Freshwater Alga *Selenastrum capricornutum*. Report number CRL F94024, T 93-10-03. Akzo Research Laboratories, Arnhem, The Netherlands.

Other

Last Changed:	May 11, 2001
Order number for sorting:	34
Remarks:	

4.4 Toxicity to Bacteria

Test Substance

Identity:	Arquad 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	86%
Remarks:	

Method

Method/guideline followed:	OECD 209 and EEC, 1988, Directive 87/392 Biodegradation
Test type:	Aquatic
GLP:	Yes
Year:	1990
Species/Source:	Activated sludge from the RZWI Nieuwgraaf in Duiven activated sludge plant
Exposure period:	30 minutes
Analytical monitoring:	No
Remarks:	Prior to use the activated sludge was diluted with tap water (1.5x) and homogenized. The concentration of the diluted activated sludge was 1.3 g dry weight/liter. 3,5-dichlorophenol (500 mg/l) was used as the positive control/reference substance.

Results

Nominal concentrations (mg/l):	0, 125, 250, 500 and 1000 mg/l
EC_{50} (30 minutes):	371 mg/l (95% confidence limits of 316 and 437 mg/l)
Remarks:	The validity of the test was shown by the consistency in the respiration rates of the controls run in conjunction with the test and reference substances and by the reference compound EC_{50} of 8.8 mg/l. The respiration rate and percent inhibition of the various concentrations of the test substance and corresponding controls are presented in the following table:

Concentration (mg/l)	Respiration Rate (mg 0_2/l/min.)	Inhibition (%)
Control 1	0.34	-
Control 2	0.36	-
125	0.32	9
250	0.27	23
500	0.11	69
1000	0.03	91

The pH of the test and control solutions at the beginning of the test ranged from 7.7 to 8.0.

Conclusions

Remarks: The activated sludge respiration inhibition test has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable without restriction, guideline study.

References

Van Ginkel, C. G and C. A. Stroo. 1990. Toxicity of Arquad 3.16 to Activated Sludge. Report number CRL F90079, T 89-09-03.1. Akzo Research Laboratories Arnhem, Arnhem, The Netherlands.

Other

Last Changed: May 14, 2001

Order number for sorting: 36

Remarks:

4.5.1 CHRONIC TOXICITY TO FISH

Test Substance

Identity:	Dodecyl trimethyl ammonium chloride (CAS RN 112-00-5)
Purity:	34.1%
Remarks:	

Method

Method/Guideline followed:	Horning, W. and C. Weber. 1985. Methods for estimating the chronic toxicity of effluents and receiving water to freshwater organisms. U. S. EPA. EPA – 600/4-85-014, 162 pp.
Test:	Static renewal
GLP:	No
Year:	1989
Species/Strain/Supplier:	Fathead minnow/Not stated/Not stated
Analytical monitoring:	Yes
Exposure period:	7-days
Statistical methods:	Not stated.
Remarks:	Concentration analysis was performed in a separate eight-week study to determine the concentration of the test substance in an artificial stream. Test substance concentrations of the stream were not analyzed during the seven-day toxicity study but a separate 8-week study was conducted to determine stability of the test concentrations in the water source. Five groups of fathead minnows were exposed to 0, 50, 250, 500 and 1250 µg/l of the test substance in river water for seven days. An additional five groups of fathead minnows were exposed to the same concentrations of the test substance in a mixture of river water and 10% final non-chlorinated sewage effluent for seven days. The river water was from the Lower East Fork of the Little Miami River, Ohio and the sewage effluent was from the Lower East Fork Sewage Treatment Plant. In an additional test conducted with river water without the test substance, five groups of fathead minnows were exposed to river water with 0, 3, 10, 30 or 100% sewage effluent. The growth and survival of the fathead minnows were analyzed for each test. The pH, dissolved oxygen and conductivity of the test solutions were determined once during each test run for the lowest, middle and highest test concentrations.

Results

Nominal concentrations (µg/l):	0, 50, 250, 500 and 1250 µg/l
Measured concentrations (µg/l):	See remarks below.
Unit:	µg/l
LOEC	> 1250 µg/l (in river water only) = 1250 µg/l (in 90% river water/10% effluent)
NOEC	> 1250 µg/l (in river water only) = 500 µg/l (in 90% river water/10% effluent)
LC_{50}	Not applicable.
Remarks:	The result of the eight-week concentration analysis study demonstrated that the concentrations of test substance in river water were within ± 15% of the target concentrations of 50, 250 and 1250 µg/l. The analysis of the control water indicated that the test substance was present at concentrations of 13 to 20 µg/l. Minnows exposed to the test substance in river water increased in weight (significantly higher than control values in the 50, 500 and 1250 µg/l groups). Survival was significantly decreased in the 250 µg/l group; however, since the decrease was not observed in a dose-dependent manner, it was not considered an effect of the test substance. Fish exposed to the test substance in 90% river water/10% wastewater treatment plant effluent did not have impaired growth at any concentration; however, survival was reduced at 1250 µg/l.

Conclusions

Remarks:	The endpoint has been adequately characterized. (ADBAC Joint Venture)

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study.

References

Davidson, D. H. 1992. Determination of the Effect of C12TMAC/Effluent Mixtures on Fathead Minnows. The Proctor & Gamble Co., Cincinnati, OH, U.S. Unpublished report (No. E89-012).

Other

Last changed:	November 16, 2001
Order number for sorting:	104
Remarks:	

4.5.1 CHRONIC TOXICITY TO FISH

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (DTDMAC); (CAS RN 68783-78-8)
Purity:	97.7%
Remarks:	The test was conducted with pure distearyl dimethyl ammonium chloride. The test substance was specially synthesized to ensure the absence of MTTMAC

Method

Method/Guideline followed:	Horning, W. B. and C. I. Weber. 1985. Short-term Methods for Estimating the Chronic Toxicity of Effluents and Receiving Waters to Freshwater Organisms. EPA-600/4-85-014. U. S. EPA, Cincinnati, Ohio.
Test:	Static renewal
GLP:	Yes
Year:	1987-1988
Species/Strain/Supplier:	Fathead minnow (*Pimephales promelas*)/In-house breeding cultures
Analytical monitoring:	Yes
Exposure period:	7-days
Statistical methods:	Probit analysis was used to calculate the lethal concentrations. For nonquantal data, effective concentrations causing a 20 percent decrease in the appropriate population level parameter and the associated 95% confidence intervals were calculated by nonlinear multiple regression analysis on SAS.
Remarks:	Acidic methanol was used as a carrier solvent in the toxicity test due to the low water solubility of the test substance. Two solvent control groups, (25 µl/l and 225 µl/l) were included the toxicity test. Filtered Little Miami River water was used for all tests. Dissolved oxygen and pH were monitored in the control and highest test concentration having survivors. The fathead minnow test was initiated with newly hatched organisms (< 24 hours old) produced from an in-house breeding culture. Fish were randomly allocated to one liter beakers containing 500 ml of test solution, ten fish per replicate, and four replicates per concentration. Fish were fed live brine shrimp four times daily and transferred to fresh test solution daily. At the end of the exposure, fish were dried and weighed. Toxicity was manifested as a decrease in survival as determined by the total dry weight of fish at the end of the study.

Results

Nominal concentrations (mg/l):	Not stated
Measured concentrations (mg/l):	0, 0.70, 2.2, 6.1, 12.7 mg/l
Unit:	mg/l
LOEC:	N/A
NOEC:	12.7 mg/l
LC_{50}:	N/A
Remarks:	A clear effect of solvent was noticeable in this toxicity test. Survival of fish in the solvent only control groups was not significantly affected; however, growth of solvent-exposed fish was reduced in a dose-dependent manner relative to naïve control fish. Effects on the growth of all test substance-exposed fish was attributed to solvent effects. Survival of the test substance-exposed fish was comparable to the survival of the fish in the untreated control group.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study.

References Shorter, S. J. 1993. The Chronic Effects of DTDMAC on the Fathead Minnow (*Pimephales promelas*) Larval Survival and Growth. Procter & Gamble Co., Cincinnati, OH, USA. Unpublished report (Report No. E89-006).

Other

Last changed:	November 16, 2001
Order number for sorting:	605
Remarks:	

4.5.2 Chronic Toxicity To Aquatic Invertebrates

Test Substance

Identity:	Dodecyl trimethyl ammonium chloride (C_{12}TMAC); (CAS RN 112-00-5)
Purity:	35%
Remarks:	

Method

Method/Guideline followed:	Not stated
Test type:	Static renewal
GLP:	No
Year:	1983-1984
Analytical procedures:	Not stated
Species/Strain:	*Ceriodaphnia sp.*
Test details:	7-Day Static renewal
Statistical methods:	Mortality data were analyzed by probit analysis to calculate the LC_{50} values. Survival was analyzed by chi-square techniques. Reproduction was analyzed by ANOVA.
Remarks:	Ohio River water was collected weekly from the shoreline at the Public Landing in downtown Cincinnati. Ohio River water physiochemical characteristics: Total hardness = 156 mg/l as $CaCO_3$; pH = 7.0 to 7.7; total suspended solids = 98 mg/l; and dissolved oxygen = 10.7. *Ceriodaphnia sp.* were acclimated to the test conditions for at least two generations before use. The LC_{50} value was based on nominal concentrations.

Results

Nominal concentrations (mg/l):	0, 0.05, 0.10, 0.20, 0.30, 0.40 and 0.60 mg/l
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
LC_{50} (7-day):	0.31 mg/l (95% confidence limit = 0.27 – 0.34 mg/l)
NOEC (mortality):	0.20 mg/l
LOEC (mortality):	0.30 mg/l
NOEC (reproduction):	0.05 mg/l
LOEC (reproduction):	0.10 mg/l
Remarks:	Concentrations of 0.40 mg/l and higher of the test substance resulted in 100% mortality. Mortality also was increased (40%) at 0.30 mg/l. Statistically significant reduction in reproduction was observed at concentrations of 0.10 mg/l and higher.

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 1B

Remarks: Reliable without restriction; comparable to guideline study.

References

Taylor, M. J. 1984. Cooperative Sensitivity of *Ceriodaphnia Sp.* and *Daphnia Magna* to Test Chemicals. Procter & Gamble Co., Cincinnati, OH, US. Unpublished report (Notebook: 25-1154, Vol., 2).

Other

Last changed: November 16, 2001

Order number for sorting: 106

Remarks:

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Dodecyl trimethyl ammonium chloride (C_{12}TMAC); (CAS RN 112-00-5)
Purity:	35%
Remarks:	

Method

Method/Guideline followed:	ASTM: Comotto, R.M. 1982. Proposed Standard Practice for Conducting Renewal Life Cycle Toxicity Test with Daphnia magna. Draft No. 1, August 1982, ASTM Committee E-47. American Society for Testing and Materials, Philadelphia, PA. and procedures outlined in Mount, D. I. And T. J. Norberg. 1983. A Seven-Day Life-Cycle Cladoceran Toxicity Test. Pre-publication. U.S. EPA (Duluth).
Test type:	Static renewal
GLP:	Not stated
Year:	1983-1984
Analytical procedures:	Not stated
Species/Strain:	*Ceriodaphnia sp.*
Test details:	7-Day static renewal
Statistical methods:	Mortality data were analyzed by probit analysis to calculate the LC_{50} values and associated 95% confidence intervals. Survival was analyzed by chi-square techniques. Reproduction was analyzed by ANOVA.
Remarks:	Water from Acton Lake was used for each test concentration. Ten 50 ml beakers containing 30 ml of test solution were used for each test concentration. Each beaker contained one *Ceriodaphnia sp.* Tests were begun with neonate *Ceriodaphnia sp.* ≤ 24 hours old. The *Ceriodaphnia sp.* were fed a diet of baker's yeast. The test lasted seven days. The young were counted and removed from each beaker daily. All test chambers were cleaned and renewed with fresh test solutions three times (on the second, fourth and sixth days). The pH and dissolved oxygen content of fresh and used test solutions were routinely monitored. All chronic toxicity values were based on nominal concentration of the test substance. The NOEC is the highest concentration that did not significantly affect the mortality, first day of reproduction or reproduction of the *Ceriodaphnia sp.*

Results

Nominal concentrations (mg/l):	0, 0.05, 0.10, 0.20, 0.30, 0.45 and 0.60 mg/l
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
LC_{50} (7-day):	0.30 – 0.45 mg/l
NOEC:	0.05 mg/l
LOEC:	0.10 mg/l
Remarks:	The physiochemical characteristics of the Acton Lake water were: Total hardness = 197 mg/l as $CaCO_3$; pH = 7.3; total suspended solids = 9.9 mg/l; and dissolved oxygen = 9.4 mg/l. Mortality was unaffected at concentrations as high as 0.30 mg/l. At 0.45 and 0.60 mg/l mortality was 90% and 100%, respectively. The first day of reproduction was significantly increased from control values for the *Ceriodaphnia sp.* exposed to test concentrations of 0.30 mg/l. Reproduction was significantly decreased compared to control values for *Ceriodaphnia sp.* exposed to test concentrations of 0.10, 0.20 and 3.0 mg/l.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study.

References

Taylor, M. J. 1984. Cooperative Sensitivity of *Ceriodaphnia Sp.* and *Daphnia Magna* to Select Surfactants. Procter & Gamble Co., Cincinnati, OH, US. Unpublished report (Notebook: ZE-1154 and ME-1082).

Other

Last changed:	November 15, 2001
Order number for sorting:	110
Remarks:	

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Dodecyl trimethyl ammonium chloride (C_{12}TMAC) (CAS RN 112-00-5)
Purity:	34.1%
Remarks:	

Method

Method/Guideline followed:	Horning, W. and C. Weber. 1985. Methods for estimating the chronic toxicity of effluents and receiving water to freshwater organisms. U. S. EPA. EPA – 600/4-85-014, 162 pp.
Test type:	Static renewal
GLP:	No
Year:	1989
Analytical procedures:	Yes
Species/Strain:	*Ceriodaphnia dubia*
Test details:	7-Day static renewal
Statistical methods:	ANOVA, Dunnett's Procedure and Fisher's Exact tests
Remarks:	Concentration analysis was performed in a separate eight-week study to determine the concentration of the test substance in an artificial stream. Test substance concentrations of the stream were not analyzed during the seven-day toxicity study. Five groups of *Ceriodaphnia dubia* were exposed to 0, 50, 250, 500 and 1250 µg/l of the test substance in river water for seven days. An additional five groups were exposed to the same concentrations of the test substance in a mixture of river water and 10% final non-chlorinated sewage effluent for seven days. The river water was from the Lower East Fork of the Little Miami River, Ohio and the sewage effluent was from the Lower East Fork Sewage Treatment Plant. An additional test was conducted with river water and varying percentages of effluent without the test substance. In this test, five groups of *Ceriodaphnia dubia* were exposed to river water with 0, 3, 10, 30 or 100% sewage effluent. The growth, survival and reproduction of *Ceriodaphnia dubia* were analyzed for each test. The pH, dissolved oxygen and conductivity of the test solutions were determined once during each test run for the lowest, middle and highest test concentrations.

Results

Nominal concentrations (µg/l):	0, 50, 250, 500 and 1250 µg/l
Measured concentrations (µg/l):	See remarks below.
Unit:	µg/l

NOEC:	50 µg/l (in river water) 250 µg/l (in river water and 10% effluent) 30 µg/l (in river water and effluent/without test substance)
LOEC:	250 µg/l (in river water) 500 µg/l (in 90% river water and 10% effluent) 100 µg/l (in river water and effluent/without test substance)
Remarks:	The result of the eight-week concentration analysis study demonstrated that the concentrations of test substance in river water were within ± 15% of the target concentrations of 50, 250 and 1250 µg/l. The analysis of the control water indicated that the test substance was present at concentrations of 13 to 20 µg/l. The results of exposure of *Ceriodaphnia dubia* to the test substance in river water are as follows: 100% mortality at 500 µg/l and higher; statistically significant decrease in survival (40% of the controls) at a concentration of 250 µg/l of the test substance; and a significant increase in reproduction at 50 µg/l. Exposure of *Ceriodaphnia dubia* to the test substance in 90% river water and 10% effluent resulted in 100% mortality at 500 µg/l and higher. The mortality in the 50 and 250 µg/l groups was 80 and 90%, respectively. There was no effect on reproduction. *Ceriodaphnia dubia* exposed to final wastewater effluent in river water (without the test substance) resulted in 0% survival at 100% effluent and increased reproduction at 30% effluent.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study.

References	Davidson, D.H. 1992. Determination of the Effect of C12TMAC/Effluent Mixtures on *Ceriodaphnia.* Procter & Gamble Co., Cincinnati, OH, USA. Unpublished report (No. E89-013).

Other

Last changed:	November 16, 2001
Order number for sorting:	107
Remarks:	

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Dodecyl trimethyl ammonium chloride (C_{12}TMAC) (CAS RN 112-00-5)
Purity:	34.1%
Remarks:	

Method

Method/Guideline followed:	Horning, W. and C. Weber. 1985. Methods for estimating the chronic toxicity of effluents and receiving water to freshwater organisms. U. S. EPA. EPA – 600/4-85-014, 162 pp.
Test type:	Static renewal
GLP:	No
Year:	1989
Analytical procedures:	Yes
Species/Strain:	*Ceriodaphnia dubia*
Test details:	7-Day Static renewal
Statistical methods:	Dunnett's Procedure and Fisher's Exact tests
Remarks:	Concentration analysis and water quality conditions were performed in a separate eight-week study to determine the concentration of the test substance in an artificial stream. Test substance concentrations of the stream were not analyzed during the study. *Ceriodaphnia dubia* were exposed to 0, 50, 250, 500 and 1250 µg/l of the test substance in 90% river water with 10% wastewater effluent in three separate studies. An additional control group was included in each test. The *Ceriodaphnia dubia* in this group were exposed to river water only. The river water was from the Lower East Fork of the Little Miami River, Ohio and the sewage effluent was from the Lower East Fork Sewage Treatment Plant. An additional test was conducted with river water and varying percentages of effluent without the test substance. The growth, survival and reproduction of *Ceriodaphnia dubia* were analyzed for each test.

Results

Nominal concentrations (µg/l):	0, 50, 250, 500 and 1250 µg/l
Measured concentrations (µg/l):	See remarks below.
Unit:	µg/l
NOEC (reproduction):	250 µg/l (in two studies and 50 µg/l in one study) 146 µg/l (geometric mean NOEC for reproduction)
NOEC (survival)	250 µg/l

LOEC (reproduction): 250 µg/l (in one of four studies and n/a in two studies)
LOEC (survival): 500 µg/l in all three groups.
Remarks: The result of the eight-week concentration analysis study demonstrated that the concentrations of test substance in river water were within ± 15% of the target concentrations of 50, 250 and 1250 µg/l. The analysis of the control water indicated that the test substance was present at concentrations of 13 to 20 µg/l. Percent survival was significantly reduced at 500 µg/l in all three tests. Reproducibility was also significantly decreased in one of the three tests. The geometric mean NOEC for reproduction was 14 µg/liter

Conclusions
Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality
Reliability (Klimisch): 1B
Remarks: Reliable without restriction; comparable to guideline study.

References

Davidson, D.H. 1992. Experimental Stream Facility Program "Experiment 1": Determination of the Effect of C12TMAC/Effluend Mixtures on Ceriodaphnia *Ceriodaphnia dubia* Procter & Gamble Co., Cincinnati, OH, USA. Unpublished report (No. E89-024).

Other
Last changed: November 14, 2001
Order number for sorting: 105
Remarks:

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Lauryl trimethyl ammonium chloride (C_{12}-TMAC) (CAS RN 112-00-5; Dodecyl trimethyl ammonium chloride)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Test type:	Flow through
GLP:	Not stated
Year:	1989-1990
Analytical procedures:	Yes
Species/Strain:	Asiatic clams (*Corbicula fluminea*)
Test details:	Flow through
Statistical methods:	Statistical evaluations of clam growth (length and weight), reproductive condition and cellulolytic enzyme activity used parametric ANOVA followed by Duncan's multiple-range test. Larval densities were evaluated by Kruskal-Wallis nonparametric one-way ANOVA. When appropriate, Student's t-tests were used to compare test and control groups.
Remarks:	Asiatic clams from three different populations and of two known morphotypes were evaluated for growth in two 8-week studies: fall 1989 and spring 1999. In the fall 1989 study, clams were collected from the Lower East Fork of the Little Miami River, OH, upstream from the wastewater treatment plant. These clams were of the white morph variety. In the spring 1990 study, clams were collected from two clean water sites: the New River, Virginia and the Sacramento River, California. These clams were white and purple morphs, respectively. Due to timing of collections, the Virginia variety were only exposed for the remaining 7-weeks of the 8- week study. Groups of 15 clams each from Ohio were evaluated in the fall study and groups of 20 clams (10 each from Virginia and California) were used in the spring study. Four streams (water from the Lower East Fork of the Little Miami River, Ohio) were used in each study. In both studies, final wastewater effluent was added to the river water at a rate to achieve a 10% final dilution by volume. In the fall study, the target test substance concentrations were 50, 250 and 1250 µg/l. The fourth stream was not treated and was used as the control. In the spring 1990 study, two streams were dosed

at 50 and 250 µg/l with a third stream remaining untreated and used as the control. A fourth stream was structurally modified such that the grade was 4% for the length of the stream to evaluate impact of stream design on micro-algal and benthic invertebrate community structure. The pH, dissolved oxygen, temperature and conductivity were measured in each stream at 5 minute intervals. Water quality was measured in both studies. Growth (length and weight), reproduction, cellulolytic enzyme activity and larval colonization of the clams were evaluated.

Results

Nominal concentrations (µg/l):	0, 50, 250 and 1250 µg/l (Fall 1989 study) 0, 50 and 250 µg/l (Spring 1990 study)
Measured concentrations (µg/l):	12.9, 49.7, 234.8 and 1151 µg/l (Fall 1989 study) 0.1, 43.2, 185.1 µg/l (Spring 1990 study)
Unit:	µg/l
NOEC (growth and mortality):	43 to 49 µg/l
LOEC (growth and mortality):	185 to 235 µg/l
Remarks:	Growth was impaired at 185 µg/l or greater for both studies and was not morphotype-dependent. Mortality, cellulolytic enzyme activity and adult reproductive condition were not altered up to concentrations of 1153 µg/l. However, larval clam (pediveliger) colonization was affected at concentrations of 43 µg/l. It is not known to what extent the effect on pediveligers would be manifested relative to recruitment to later life stages.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch):	1D
Remarks:	Reliable without restriction; special study design.

References

Belanger, S.E., D. H. Davidson, J. L. Farris, D. Reed, and D. S. Cherry. 1993. Effects of Cationic Surfactant Exposure to a Bivalve Mollusc in Stream Mesocosms. Environmental Toxicology and Chemistry, 12:1789-1802.

Other

Last changed:	November 16, 2001
Order number for sorting:	101
Remarks:	

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Dodecyl trimethyl ammonium chloride (CAS RN 112-00-5)
Purity:	99.7%
Remarks:	

Method

Method/Guideline followed:	Modifications of the method of Snell, T. W. and B. D. Moffat. 1992. A 2-d life cycle test with the rotifer *Brachionus calyciflorus. Environ. Contam. Toxicol.* **26**:549-554.
Test type:	Static
GLP:	Not stated
Year:	1996
Analytical procedures:	Yes
Species/Strain:	*Brachionus calyciflorus*
Test details:	Static
Statistical methods:	The 48-hour EC_{20} and EC_{50} values with associated 95% confidence intervals were estimated by the iterative nonlinear regressions test. All statistical tests were performed with SAS®, version 6.0.
Remarks:	Tests were conducted with *Brachionus calyciflorus* obtained from Bioresponse Systems, Inc. (Halifax, NS, Canada). For each test, approximately 3,000 cysts were hydrated with dilution water 20 hour prior to test initiation. Three replicates, each containing six newly hatched swimming rotifers in 10 ml of test water, were used for each test concentration and control. Each test consisted of four to six test concentrations, a control replicate and a solvent control replicate, if appropriate. The dilution water was a 50/50 blend of locally obtained well water and deionized water and had mean water quality properties of: pH 8.6, dissolved oxygen 8.5, hardness 152 mg/l as $CaCO_3$ and conductivity 450 µmhos. Rotifers were counted after 48 hours in all control and test concentration replicates. This publication presents data for a large number of surfactants and does not specify concentrations used for each chemical. The value is included in the dataset due to the importance of the publication in providing framework for QSAR models of aquatic toxicity.

Results

Nominal concentrations (mg/l): Not stated.
Measured concentrations (mg/l): Not stated.
Unit: mg/l
NOEC/LOEC: Not stated
Remarks: EC_{20} = 0.19 mg/l
(with 95% confidence interval of 0.179 – 0.225 mg/l)
EC_{50} = 0.23 mg/l
(with 95% confidence interval of 0.212 – 0.246 mg/l)

Due to the rapid sorption and degradation of surfactants during static toxicity tests, test concentrations decreased during the two-day test by 20 to 90%, necessitating the use of time-weighted average exposure concentrations.

Conclusions

Remarks: The data are useful in support of the overall category. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 2A
Remarks: Reliable with restriction; acceptable, well-documented publication.

References

Versteeg, D. J., D. T. Stanton, M. A. Pence and C. Cowan. 1997. Effects of Surfactants on the Rotifer, *Brachionus Calyciflorus*, in a Chronic Toxicity Test and in the Development of QSARS. Environmental Toxicology and Chemistry, 16:1051-1058.

Other

Last changed: November 16, 2001
Order number for sorting: 108
Remarks:

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Hexadecyl trimethyl ammonium chloride (CAS RN 112-02-7)
Purity:	> 95%
Remarks:	

Method

Method/Guideline followed:	Modifications of the method of Snell, T. W. and B. D. Moffat. 1992. A 2-d life cycle test with the rotifer *Brachionus calyciflorus*. *Environ. Contam. Toxicol.* **26**:549-554.
Test type:	Static
GLP:	Not stated
Year:	1996
Analytical procedures:	Yes
Species/Strain:	*Brachionus calyciflorus*
Test details:	Static
Statistical methods:	The 48-hour EC_{20} and EC_{40} values with associated 95% confidence intervals were estimated by the iterative nonlinear regressions test. All statistical tests were performed with SAS®, version 6.0.
Remarks:	Tests were conducted with *Brachionus calyciflorus* obtained from Bioresponse Systems, Inc. (Halifax, NS, Canada). For each test, approximately 3,000 cysts were hydrated with dilution water 20 hour prior to test initiation. Three replicates, each containing six newly hatched swimming rotifers in 10 ml of test water, were used for each test concentration and control. Each test consisted of four to six test concentrations, a control replicate and a solvent control replicate, if appropriate. The dilution water was a 50/50 blend of locally obtained well water and deionized water and had mean water quality properties of: pH 8.6, dissolved oxygen 8.5, hardness 152 mg/l as $CaCO_3$ and conductivity 450 µmhos. Rotifers were counted after 48 hours in all control and test concentration replicates. This publication presents data for a large number of surfactants and does not specify concentrations used for each chemical. The value is included in the dataset due to the importance of the publication in providing framework for QSAR models of aquatic toxicity.

Results

Nominal concentrations (mg/l): Not stated.
Measured concentrations (mg/l): Not stated.
Unit: mg/l
NOEC/LOEC: Not stated
Remarks: EC_{20} = 0.053 mg/l
(with 95% confidence interval of 0.0447 – 0.0619 mg/l)
EC_{50} = 0.067 mg/l
(with 95% confidence interval of 0.0612 – 0.0732 mg/l)

Due to the rapid sorption and degradation of surfactants during static toxicity tests, test concentrations decreased during the two-day test by 20 to 90%, necessitating the use of time-weighted average exposure concentrations.

Conclusions

Remarks: The data are useful in support of the overall category. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 2A
Remarks: Reliable with restriction; acceptable, well-documented publication.

References

Versteeg, D. J., D. T. Stanton, M. A. Pence and C. Cowan. 1997. Effects of Surfactants on the Rotifer, *Brachionus Calyciflorus*, in a Chronic Toxicity Test and in the Development of QSARS. Environmental Toxicology and Chemistry, 16:1051-1058.

Other

Last changed: November 16, 2001
Order number for sorting: 201
Remarks:

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Test Substance

Identity:	Monotallowtrimethyl ammonium chloride (CAS RN 8030-78-2; quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	non-radiolabeled: 48.4%
Remarks:	Stock solutions were prepared using non-radiolabeled test substance and radiolabeled. ^{14}C-Alkyl Stearyl trimethyl ammonium chloride (^{14}C-STAC) in isopropanol. Purity of ^{14}C-STAC was 98%.

Method

Method/Guideline followed:	Not stated
Test type:	Static (daily renewal)
GLP:	Not stated
Year:	1980-1981
Analytical procedures:	Yes
Species/Strain:	*Daphnia magna*/Not stated
Test details:	Static daily renewal
Statistical methods:	Mortality data were analyzed by probit analysis to derive a 21-day LC_{50} value and associated 95% confidence interval. T-tests were used to analyze statistically significant differences in other tested parameters including days to first reproduction, total young production, mean brood size, and 21-day length.
Remarks:	*Daphnia magna* (< 24 hours old) were exposed to six concentrations of the test substance in a 21-day static-daily renewal test. Control and isopropanol control (IPA) groups were also evaluated. Three water types were utilized in this test: laboratory blended water (total hardness ~150 mg/l), Southwest well water (total hardness ~350 mg/l) and river water (total hardness ~300-350 mg/l). The river water, exemplifying a natural surface water that received sewage effluent, was collected from the White River (Indiana) and transported for cold storage (~4°C). The test in blended water was discontinued after 14 days due to inadequate reproduction by control organisms. Mortality was monitored daily and the number of young produced in each beaker was recorded after which they were discarded. Temperature was recorded daily and pH, dissolved oxygen and hardness were determined on alternate days in control waters, both fresh and 24 hours old. Daphnid 21-day length was also determined by the use of an ocular micrometer measuring from the base of the spine to the apex of the helmet. Because no statistically significant

differences in Daphnid length occurred as a result of exposure to increasing concentrations of the test substance, this parameter was not measured in the well water.

Results

Nominal concentrations (µg/l): in Southwest well water: 2.5, 5.0, 10.0, 20.0, 40.0 and 80.0 µg/l
in River water: 74.4, 110.4, 146.4, 218.4, 290.4, 578.4 µg/l

Measured concentrations (µg/l): Values represent the geometric mean of the 0- and 24-hour concentration analyses:
Southwest well water: 1.6, 3.1, 6.8, 14.6, 30.6 and 60.8 µg/l
River water: 35.7, 53.4, 68.3, 99.1, 122.3 and 309.3 µg/l

Unit: µg/l

NOEC/LOEC: Southwest well water: NOEC = 6.8 µg/l
River water: NOEC = 99.1 µg/l

Remarks: Distribution and removal studies were conducted prior to the acute toxicity tests. Because of the very rapid removal of the test substance from the water column, the geometric mean of the 0- and 24-hour concentrations was considered to be the overall exposure concentration in the chronic toxicity tests. The water chemistries remained relatively constant during the test periods.

Southwest well water test			
Measured Concentration (µg/l)	**% Mortality**	**Total Young Produced**	**Mean Brood Size**
Control	10	690	7
IPA Control	5	699	7
1.6	10	670	7
3.1	6	531	6
6.8	15	649	7
14.6	42	384*	6
30.6	50*	509*	10
60.3	100*	----	----

* = significantly different from IPA control ($p < 0.05$)

White River Water Test				
Measured Concentration (µg/l)	**% Mortality**	**Total Young Produced**	**Mean Brood Size**	**21-Day Length (mm)**
Control	5	1292	10	3.6
IPA Control	5	1365	12	3.5
35.7	5	1295	11	3.6
53.4	5	1292	10	3.4
68.3	0	1292	10	3.4
99.1	0	1107	9	3.2
122.0	20	1049*	11	3.2
309.3	100*	----	----	----

* = significantly different from IPA control ($p < 0.05$)

The number of days until the first reproduction was similar across all groups within the Southwest well water test and White River water test, (11 days and 8-9 days, respectively.)

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 1B

Remarks: Reliable without restriction; comparable to guideline study.

References

Valentine, L. C. and W. E. Bishop. 1992. Effects of MTTMAC on the Survival and Reproduction of *Daphnia Magna* in Laboratory Waters and a Natural Surface Water. Procter & Gamble Co., Cincinnati, OH, USA. Unpublished report (Notebook: ME-5004, ME-5007 and ZE-1111).

Other

Last changed: November 16, 2001

Order number for sorting: 301

Remarks:

4.5.2 Chronic Toxicity To Aquatic Invertebrates

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (DTDMAC); (CAS RN 68783-78-8)
Purity:	97.7%
Remarks:	The test was conducted with pure distearyl dimethyl ammonium chloride. The test substance was specially synthesized to ensure the absence of MTTMAC

Method

Method/guideline followed:	Horning, W. B. and C. I. Weber. 1985. Short-term Methods for Estimating the Chronic Toxicity of Effluents and Receiving Waters to Freshwater Organisms. EPA-600/4-85-014. U. S. EPA, Cincinnati, Ohio.
Type:	Static renewal
GLP:	Yes
Year:	1987-1988
Analytical monitoring:	Yes
Species/Strain:	*Ceriodaphnia dubia*
Test details:	7 days
Statistical methods:	Probit analysis was used to calculate the lethal concentrations. For nonquantal data, effective concentrations causing a 20 percent decrease in the appropriate population level parameter and the associated 95% confidence intervals were calculated by nonlinear multiple regression analysis on SAS.
Remarks:	Acidic methanol was used as a carrier solvent in the toxicity test due to the low water solubility of the test substance. A solvent control group was included with each toxicity test. Filtered Little Miami River water was used for all tests. Dissolved oxygen and pH were monitored in the control and highest test concentration having survivors. The *Ceriodaphnia* were tested with neonates (< 16 hours old) by placing them into individual plastic cups containing 20 ml of test solution. Organisms were transferred into new test solution and fed a fermented fish food/yeast diet, daily. Number of young produced and survival of adults were followed through the end of the test on day 7. Toxicity was measured as an effect on young production or mortality as compared with the control group.

Results

Nominal concentrations (mg/l):	Not stated
Measured concentrations (mg/l):	0, 0.06, 0.12, 0.21, 0.41, 0.78 and 0.90 mg/l
Unit:	mg/l
LC_{50} (7-day):	0.70 mg/l (95% confidence limit 0.516 – 1.00 mg/l)
NOEC (7-day):	Not stated (approximately 0.21 mg/l)
LOEC (7 day):	Not stated (approximately 0.41 mg/l
Remarks:	Ceriodapnia reproduction was decreased by exposure to the solvent; therefore, the effects of the test substance on reproduction were compared to the solvent control group. Survival of *Ceriodaphnia* was 100% at concentrations as high as 0.21 mg/l. Percent survival at 0.41, 0.78 and 1.90 mg/l was 80%, 50% and 0%, respectively. The test substance resulted in a dose-dependent decrease in reproduction (an EC_{20} of 0.26 mg/l was calculated for this reproductive effect). The effects on *Ceriodaphnia* in this study were greater than other studies probably due to levels of solids in the test medium resulting in differences in bioavailability.

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study.

References

Shorter, S. J. 1993. The Chronic Effects of DTDMAC on the Fathead Minnow (*Pimephales promelas*) Larval Survival and Growth. Procter & Gamble Co., Cincinnati, OH, USA. Unpublished report (Report No. E89-006).

Other

Last changed:	November 16, 2001
Order number for sorting:	605
Remarks:	

4.5.2 Chronic Toxicity To Aquatic Invertebrates

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (DTDMAC); (CAS RN 68783-78-8)
Purity:	71.4%
Remarks:	

Method

Method/Guideline followed:	ASTM: Comotto, R.M. 1982. Proposed Standard Practice for Conducting Renewal Life Cycle Toxicity Test with Daphnia magna. Draft No. 1, August 1982, ASTM Committee E-47. American Society for Testing and Materials, Philadelphia, PA. and procedures outlined in Mount, D. I. And T. J. Norberg. 1983. A Seven-Day Life-Cycle Cladoceran Toxicity Test. Pre-publication. U.S. EPA (Duluth).
Test type:	Static renewal
GLP:	Not stated
Year:	1983-1984
Analytical procedures:	Not stated
Species/Strain:	*Ceriodaphnia sp.*
Test details:	7-Day Static renewal
Statistical methods:	Mortality data were analyzed by probit analysis to calculate the LC_{50} values and associated 95% confidence intervals. Survival was analyzed by chi-square techniques. Reproduction was analyzed by ANOVA.
Remarks:	Two chronic toxicity tests were performed with *Ceriodaphnia sp.* under the following conditions: 1) test conducted in Acton Lake water and the *Ceriodaphnia sp.* fed a diet of baker's yeast; and 2) test conducted in Ohio River water and the *Ceriodaphnia sp.* fed a diet consisting of a mixture of algae, trout chow and alfalfa. Ten 50 ml beakers containing 30 ml of test solution were used for each test concentration. Each beaker contained one *Ceriodaphnia sp.* Tests were begun with neonate *Ceriodaphnia sp.* ≤ 24 hours old. The test lasted seven days. The young were counted and removed from each beaker daily. All test chambers were cleaned and renewed with fresh test solutions three times (on the second, fourth and sixth days). The pH and dissolved oxygen content of fresh and used test solutions were routinely monitored. All chronic toxicity values were based on nominal concentration of the test substance. The NOEC is the highest concentration that did not significantly

affect the mortality, first day of reproduction or reproduction of the *Ceriodaphnia sp.*

Results

Nominal concentrations (mg/l):	in Acton Lake water: 0, 0.10, 0.25, 0.50, 0.78, 1.0, 2.0, 3.0 and 4.0 mg/l in Ohio River water: 0, 0.025, 0.050, 0.1, 0.2, 0.5, 1.0, 2.0 and 3.0 mg/l
Measured concentrations (mg/l):	Not stated
Unit:	mg/l
LC_{50} (7-day):	in Acton Lake water: 0.82 mg/l (95% confidence limit of 0.43- 1.04 mg/l) in Ohio River water: 0.82 mg/l (95% confidence limit of 0.58 - 1.1 mg/l)
NOEC:	in Acton Lake water: 0.10 mg/l in Ohio River water: 0.10 mg/l
LOEC:	in Acton Lake water: 0.25 mg/l in Ohio River water: 0.20 mg/l
Remarks:	The physiochemical characteristics of the Acton Lake water were: Total hardness = 197 mg/l as $CaCO_3$; pH = 7.3; total suspended solids = 9.9 mg/l; and dissolved oxygen = 9.4 mg/l. The physiochemical characteristics of the Ohio River water were: Total hardness = 110 mg/l as $CaCO_3$; pH = 7.4; total suspended solids = 87 mg/l; and dissolved oxygen = 9.7 mg/l. Results of *Ceriodaphnia sp.* exposure to the test substance in Acton Lake Water: Survival was significantly reduced at concentrations of 0.75 mg/l and higher when compared to controls. Mortality was 40%, 80% 100%, 100% and 100% at concentration of 0.75, 1.0, 2.0, 3.0 and 4.0 mg/l, respectively. A statistically significant increase in the first day of reproduction was noted at the 0.25, 0.50 and 0.75 mg/l concentrations. Statistically significant reductions in reproduction were noted at the 0.10, 0.50 and 0.75 mg/l concentrations compared to the control group values. However, since reproduction was not affected at a concentration of 0.25 mg/l the reduction noted at 0.10 mg/l was not considered related to the test substance. Results of *Ceriodaphnia sp.* exposure to the test substance in Ohio River water: Survival was significantly reduced at test substance concentrations of 1.0 mg/l and higher when compared to controls. Mortality was 70% 100% and 100% at concentration of 1.0, 2.0 and 3.0 mg/l, respectively. Statistically significant increases in the first day of reproduction were noted at the 0.050 and 0.5 mg/l concentrations; however, since these increases were not

seen in a dose-related fashion, they were not considered an effect of the test substance. Statistically significant reductions in reproduction were noted at the 0.2. 0.5 and 1.0 mg/l concentrations compared to the control group values.

Conclusions

Remarks: The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group)

Data Quality

Reliability (Klimisch): 1B

Remarks: Reliable without restriction; comparable to guideline study.

References

Taylor, M. J. 1984. Cooperative Sensitivity of *Ceriodaphnia Sp.* and *Daphnia Magna* to Select Surfactants. Procter & Gamble Co., Cincinnati, OH, US. Unpublished report (Notebook: ZE-1154 and ME-1082).

Other

Last changed: November 16, 2001

Order number for sorting: 603

Remarks:

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Test Substance

Identity:	Arquad 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	87.9 %
Remarks:	None

Method

Method/Guideline followed:	OECD Guidelines for Testing of Chemicals, *Daphnia*, Reproduction Test, Test Guideline 202, Part II, draft 1993
Test type:	Semi-static
GLP:	Yes
Year:	1995
Analytical procedures:	Yes
Species/Strain:	*Daphnia magna*/Clone V, originally obtained from the RIZA, Lelystad, The Netherlands
Test details:	Semi-static, test solutions renewed three times per week
Statistical methods:	Using the statistical package SAS (SAS version 6.09, SAS Institute Inc., Cary, NC, USA)
Remarks:	Based on the results of two preliminary tests, groups of 20 young female *Daphnia*, less than 24 hours at the start of the test, were exposed to the test substance at nominal concentrations of 0.01, 0.02, 0.04, 0.08, 0.16 and 0.32 mg/l in a 21-day semi-static renewal chronic toxicity test. A control group (20 *Daphnia*) was tested without the test substance. Immobilization (or death) and reproduction (number of young produced per parent animal) were the criteria used to determine the concentration of the test substance in water that produced an adverse effect on the test organism over the 21-day test period. Four test vessels (400 ml beaker, 250 ml volume of test solution per vessel) per test concentration were employed and each test vessel contained five animals. The test substance was known to have a high affinity for glass surfaces; therefore, the test vessels were pretreated with the respective test solutions. Stock solutions containing the test substance and deionized water, were prepared before the start of the test. Test solutions were freshly prepared on the day of medium renewal. The test solutions were not aerated during the test; instead, the dilution water was aerated prior to use for test solution preparation. During the test period, the test solutions were renewed three times a week. To determine the actual concentrations of the test substance chemical

analyses were performed in fresh and old test solutions from the 0, 0.02, 0.08 and 0.16 mg/l dose levels in week 1 and week 3. During the course of the test, relevant parameters such as the time to production of the first brood and the mortality of the parent animals were recorded. At the end of the treatment period, the mean number of living offspring per parent animal per day from the start of the test was assessed. The reproductive output of the animals exposed to the test chemical at each concentration was compared to that of the control. The photoperiod was 16 hours light and 8 hours dark, the light intensity was approximately 950 lux. The pH ranged from 7.5 to 8.5. Temperature measured at the days of medium renewal in the old and the fresh test solutions ranged from 19.4 to 20.8 ºC. Dissolved oxygen ranged from 8.1 to 10.0 mg/l.

Results

Nominal concentrations (mg/l): 0, 0.01, 0.02, 0.04, 0.08, 0.16 and 0.32 mg/l

Measured concentrations (mg/l):

		Nominal concentrations (mg technical product/l)			
		Control	0.02	0.08	0.16
Test day	**Sample type**	**Measured concentrations (mg technical product/l)**			
3	Fresh	0.000	0.023	0.082	0.138
5	Old	0.000	0.018	0.093	0.187
17	Fresh	0.001	0.028	0.096	0.169
19	Old	0.001	0.026	0.084	0.197

Unit: mg/l

NOEC

(nominal concentrations): Mortality of parent animals = 0.04 mg/l
Reproduction (living offspring) = 0.04 mg/l
Time of production of first brood = 0.08 mg/l

(measured concentrations): Mortality of parent animals = 0.064 mg/l
Reproduction (living offspring) = 0.064 mg/l
Time of production of first brood = 0.128 mg/l

LOEC

(nominal concentrations): Mortality of parent animals = 0.08 mg/l
Reproduction (living offspring) = 0.08 mg/l
Time of production of first brood = 0.16 mg/l

(measured concentrations): Mortality of parent animals = 0.128 mg/l
Reproduction (living offspring) = 0.128 mg/l
Time of production of first brood = 0.256 mg/l

Statistical results: Described above

Remarks: Following is the cumulative percent mortality:

Nominal concentration (mg/l)	% Mortality Test day							
	0	3	5	7, 10	12	14	17, 19	21
0.0	0	0	0	0	5	5	5	5
0.01	0	5	10	10	10	10	10	10
0.02	0	0	0	0	0	5	5	5
0.04	0	0	0	0	0	5	5	5
0.08	0	20	30	30	35	35	40	45
0.16	0	35	60	70	70	70	70	70
0.32	0	100	-	-	-	-	-	-

All concentrations higher than 0.04 mg/l caused a significant inhibition as compared to the control, and all concentrations up to and including 0.04 mg/l did not. In the range of concentrations between 0.01 and 0.04 mg/l the response was not monotone. This was likely to be caused by the very low test concentrations and problems due to the strong affinity of the test substance to glass surfaces. At all concentrations up to and including 0.08 mg/l, the first brood was observed at day 10 of the test, while the first brood at 0.16 mg/l was observed on day 12. The percent recovery of all analyses performed at all concentrations during the test ranged from 121 to 200 and the mean percent recovery over all analyses was 160 ± 22. The relatively high measured concentrations were likely to be caused by one or both of the following circumstances: 1) the extreme low concentrations required a 1000x concentration step; 2) as the test vessels were pretreated with the test substance, it could not be excluded that the test substance bound to the surface of the test vessels during pretreatment and was partially or completely released during the extraction step and thereby increased the analyses values. The additional amount of test substance due to the pretreatment may have resulted in a higher actual concentration found in the analyses, but it was unlikely that this additional amount of test substance also was bioavailable in the test solution. Based on the results of chemical analyses it was very likely that the nominal concentrations were maintained during the test.

Conclusions

Remarks: The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; guideline study.

References

Mark, U. E. 1995. Chronic Toxicity of Arquad 3.16 to *Daphnia magna*. Report number CRL F94086, T 93-10-03. Akzo Research Laboratories Arnhem, Arnhem, The Netherlands.

Other

Last changed: May 14, 2001

Order number for sorting: 31

Remarks:

5.1.1 ACUTE ORAL TOXICITY

Test Substance

Identity: P1232 (CAS RN 112-00-5; Ammonium, dodecyltrimethyl-, chloride).

Purity: 24.7% aqueous solution

Remarks:

Method

Method/Guideline followed: Not stated

Type: LD_{50}

GLP: Yes

Year: 1982

Species/Strain: Sprague Dawley CD rats

Sex: Male and female

No. of animals per sex per dose: 5

Vehicle: Undiluted

Route of administration: Oral gavage

Remarks: Five male and five female rats per group were administered the test substance at 0.19, 0.26, 0.36, 0.51, 0.71, or 1.00 ml/kg via gavage. The test substance was dosed as supplied (24.7% aqueous solution). Prior to dosing, the rats were deprived of food for 18-20 hours. The animals were returned to *ad libitum* feeding immediately after dosing. The animals were observed for mortality and pharmacotoxic symptoms at frequent intervals during the first 4 hours after dosing and daily thereafter for the next 14 days.

Results

Value: LD_{50} = 490 mg/kg (420-570 mg/kg 95% confidence interval)

Number of deaths:

Dose (ml/kg)	Male Deaths	Female Deaths
0.19	0/5	0/5
0.26	0/5	0/5
0.36	0/5	1/5
0.51	3/5	3/5
0.71	4/5	5/5
1.00	5/5	5/5

Remarks: None

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study

References Hiles, R.A. 1982. Acute oral toxicity (LD_{50} value in rats). Springborn Institute for Bioresearch, Inc. Spencerville, OH, USA. Unpublished report 3029.976.

Other

Last changed:	September 12, 2001
Order number for sorting:	2c1
Remarks:	

5.1.1 ACUTE ORAL TOXICITY

Test Substance

Identity: C12TMAC (CAS RN 112-00-5; Ammonium, dodecyltrimethyl-, chloride).
Purity: 37.35% aqueous solution
Remarks:

Method

Method/Guideline followed: Not stated
Type: Acute toxicity
GLP: Yes
Year: 1983
Species/Strain: Sprague Dawley CD rats
Sex: Male and female
No. of animals per sex per dose: 5
Vehicle: Undiluted or water for lower doses (25% solution)
Route of administration: Oral gavage
Remarks: Five male and five female rats per group were administered the test substance at 0.29, 0.40, 0.56, 0.78, 1.09, 2.14, or 3.00 g/kg via gavage. The four highest doses were tested with the test substance as supplied (37.35% aqueous solution) and the three lowest doses were further diluted with water. A control group receiving 10 ml/kg of distilled water was included. Prior to dosing, the rats were deprived of food for 18-20 hours. The animals were returned to ad libitum feeding immediately after dosing. The animals were observed for mortality and pharmacotoxic symptoms at frequent intervals during the first 4 hours after dosing and daily thereafter for the next 14 days. A gross necropsy was performed on all animals.

Results

Value: LD_{50} = 560 mg/kg (500-630 mg/kg 95% confidence interval)

Number of deaths:

Dose (g/kg)	Male Deaths	Female Deaths
0.29	0/5	0/5
0.40	0/5	0/5
0.56	2/5	3/5
0.78	5/5	5/5
1.09	5/5	5/5
2.14	5/5	5/5
3.00	5/5	5/5

Remarks:

Conclusions

Remarks: The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1B

Remarks: Reliable without restrictions; comparable to guideline study

References

Newmann, E. A. 1983. Acute oral toxicity (LD_{50}) study, B83-0040, BTS 2864, P1324. Procter & Gamble Co. Cincinnati, OH, USA. Unpublished report (No. B83-0040).

Other

Last changed: September 13, 2001

Order number for sorting: 2c

Remarks:

5.1.1 Acute Oral Toxicity

Test Substance

Identity:	Hexadecyl trimethyl ammonium chloride (CAS RN 112-02-7; Ammonium, hexadecyltrimethyl-, chloride).
Purity:	100%
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	Acute toxicity
GLP:	Not stated
Year:	1978 - 1979
Species/Strain:	Swiss-Webster mice
Sex:	Male and female
No. of animals per sex per dose:	5 mice
Vehicle:	Sterile water
Route of administration:	Oral gavage
Remarks:	Five male and five female mice approximately 15 to 30 g at study initiation were administered 300 - 600 mg/kg of the test substance by oral gavage. Concentrations of the dosing solutions were 4.8% w/w. [Note: Although not specified, it was assumed that the doses were corrected to active ingredient based on consistency with data for similar test materials]. Sterile water was used in the preparation of all solutions. Prior to dosing, the mice were fasted from food for approximately 16 - 20 hours. Food was returned approximately 3 - 4 hours post-dose. All animals were observed closely during the first few hours after dosing and at least twice each hour thereafter during the first working day. Animals were then observed once daily for a total of seven days. Necropsies were performed on some mice that died following administration of the test compound. Gross necropsy findings were not always recorded, depending on the finding and/or motivation for performing the necropsy i.e. to determine if the material had been properly administered, to determine the level of stomach irritation and/or determine the cause of death, etc.

Results

Value:	LD_{50} = Not determined (400 mg/kg < LD_{50} < 600 mg/kg)
Number of deaths:	400 mg/kg = 3/10 600 mg/kg = 10/10
Remarks:	Symptoms produced were primarily ataxia and loss of righting reflex. Hexadecyl trimethyl ammonium chloride (500 mg/kg) showed an average symptom onset time of 67 minutes with all the animals dying at this dose level. Continuous observation showed that a normal appearing animal would assume a prone position and then die within seconds. Delayed deaths (those occurring one or more days following dose administration) were observed. This resulted in the minimum lethal dose being below the dose that produced visible neurotoxic symptoms. The delayed deaths were possibly related to the irritancy of the test substance. All deaths occurred within 96 hours of treatment. Gross necropsy of mice that died shortly after treatment revealed no abnormalities.

Conclusions

Remarks:	The acute oral LD_{50} has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References

Nixon, C. A., B. E. Domeyer, P. J. Reer and M. E. Volpenheim. 1981. Visible Neurotoxic Effects of a Series of Purified and Commercial Grade Quaternary Ammonium Compounds and Alkylethoxylate Nonionics Following Oral Administration to Dogs, Rabbits and Mice. Study number: 1089-26077. Procter & Gamble, Cincinnati, OH, U. S.

Other Available Reports

Other

Last changed:	December 13, 2001
Order number for sorting:	6
Remarks:	

5.1.1 Acute Oral Toxicity

Test Substance

Identity:	ARQUAD T-50 (CAS RN 8030-78-2; Quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	OECD 401
Type:	LD_{50}
GLP:	Yes
Year:	1986
Species/Strain:	Sprague-Dawley CFY rat
Sex:	Male and female
No. of animals per sex per dose:	5
Vehicle:	None
Route of administration:	Oral gavage
Remarks:	Five male and five female rats per group, approximately 5 to 8 weeks old and 130 – 162 g (males) and 123 – 151 g (females) at study initiation were administered 1000, 1260, 1587 or 2000 mg/kg of the test substance by oral gavage. The animals were fasted overnight prior to dosing and for approximately two hours after dosing. The rats were observed 1 and 4-hours after dosing and once daily for 14 days. Mortality and evidence of overt toxicity were recorded at each observation. Body weights were recorded at 0, 7 and 14 days and at death. All animals were subjected to gross necropsy examinations for any macroscopic abnormalities. No tissues were retained. The LD_{50} was calculated using the method of Weil, C.S. (1952), Biometrics 8, 249. A separate LD_{50} value was calculated for male but the mortality data did not allow calculation of a separate value for females and a best estimate was given.

Results

Value:	LD_{50} (combined) = 1260 mg/kg (95% confidence limits = 1061 to 1496 mg/kg) LD_{50} (males) = 1289 mg/kg (95% confidence limits = 1151 to 1444 mg/kg) LD_{50} (females) = best estimate between 1000 and 2000 mg/kg

Number of deaths:	1000 mg/kg = 0 males, 2 females 1260 mg/kg = 2 males, 4 females 1587 mg/kg = 5 males, 2 females 2000 mg/kg = 5 males, 4 females
Remarks:	One male and one female treated with 1587 mg/kg died on the day of dosing; all other deaths were noted one to four days after dosing. Major signs of toxicity noted in decedent and surviving animals in all groups were hunched posture, lethargy, piloerection, decreased respiratory rate and diarrhea. Animals treated with 1260 mg/kg and above showed additional signs including: ataxia, tip-toe gait, ptosis, pallor of the extremities, increased lacrimation, chromodacryorrhea, diuresis, occasional body tremors, emaciation and red/brown staining around the snout. All survivors from the 1000 mg/kg group appeared normal beginning on day 3; animals treated with 1260 and 1587 mg/kg appeared normal by day 5; and the single survivor from the 2000 mg/kg dose group showed signs of toxicity until day 12. Effects on body weight gain were commonly noted in animals treated with 1260 mg/kg and above at day 7 but all survivors made expected body weight gains during the second week. Necropsy of decedents revealed abnormally red lungs, dark livers, hemorrhage and ulceration of the gastric mucosa and congestion of the small intestines. Surviving animals necropsied at termination showed white raised areas on the non-glandular region of the stomach or general white thickening of this region. Isolated animals from the 1260 and 2000 mg/kg dose groups showed adhesions of the stomach to the abdominal wall and/or liver.

Conclusions

Remarks:	The acute oral LD_{50} has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; guideline study.

References

Jones, J. R., M. P. Blackwell and T. A. Collier. 1986. ARQUAD T-50: OECD 401 Acute Oral Toxicity Test in Rat. Project number 106/4. Safepharm Laboratories Limited, Derby, U. K.

Other Available Reports

Other

Last changed: December 13, 2001
Order number for sorting: 13a
Remarks:

5.1.1 Acute Oral Toxicity

Test Substance

Identity:	Monostearyl trimethyl ammonium chloride (CAS RN 112-03-8; Trimethyloctadecylammonium chloride)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	Acute toxicity
GLP:	Not stated
Year:	1989
Species/Strain:	ddY mice
Sex:	Male and female
No. of animals per sex per dose:	10 mice per dose (article does not specify proportion of male and female animals)
Vehicle:	None
Route of administration:	Oral
Remarks:	Animals were fasted from food for 15 hours prior to dosing and six hours following dosing. Animals were monitored for the number of deaths for 14 days following dose administration. Necropsies were performed immediately after death or at terminal sacrifice on Day 14. The LD50 was calculated using the Litchfield and Wilcoxon method (Litchfield, J. T. and F. Wilcoxon. 1949. J. Pharmacol. Ther. 96:99).

Results

Value:	LD_{50} (males) = 633 mg/kg (95% confidence limits = 550 to 728 mg/kg) LD_{50} (females) = 536 mg/kg (95% confidence limits = 476 to 600 mg/kg)
Number of deaths:	Not stated.
Remarks:	Symptoms produced were hypoactivity and diarrhea. Necropsy findings included congestion of brain and kidney.

Conclusions

Remarks:	The acute oral LD_{50} has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References

Hasegawa, R., Y. Nakaji, Y. Kurokawa and M. Tobe. 1989. Acute Toxicity Tests on 113 Environmental Chemicals. Sci. Rep. Res. Inst. Tohoku Univ., -C. (36)1-4:10-16.

Other Available Reports

Other

Last changed:	December 13, 2001
Order number for sorting:	10a1
Remarks:	

5.1.1 Acute Oral Toxicity

Test Substance

Identity:	ARQUAD M2HTB-85 (CAS RN 61789-77-3; Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	LD_{50}
GLP:	Not stated
Year:	1980
Species/Strain:	Harlan Sprague-Dawley rat
Sex:	Male and female
No. of animals per sex per dose:	8
Vehicle:	None
Route of administration:	Oral gavage
Remarks:	Eight male and eight female rats, approximately 8 weeks old and 200 - 300 g at study initiation. The animals were fasted overnight prior to dosing. The rats were observed for pharmacotoxic signs and mortality at 1, 2.5 and 4 hours after dosing. For 14 days thereafter animals were observed once daily for pharmacotoxic signs and twice daily for mortality. Body weights were recorded just prior to dosing and at 7 and 14 days after dosing. At study termination, surviving animals were euthanized. Animals that died during the study or were euthanized received a gross necropsy examination and abnormalities were recorded.

Results

Value:	LD_{50} (combined) = 0.96 g/kg (95% confidence limits = 0.63 to 1.47 g/kg) LD_{50} (males) = 0.93 g/kg (95% confidence limits = 0.75 to 1.14 g/kg) LD_{50} (females) = 1.00 g/kg (95% confidence limits = 0.25 to 4.09 g/kg)
Number of deaths:	0.27 g/kg = 0 males; 0 females 0.43 g/kg = 0 males; 0 females 0.67 g/kg = 3 males; 5 females 1.05 g/kg = 6 males; 5 females 1.31 g/kg = 6 males; 4 females 2.05 g/kg = 8 males; 8 females 3.20 g/kg = 8 males; 8 females

Remarks: Due to the flatness of the curve in the mortality rate of both sexes, 95% confidence limits of 20% or less could not be derived. The decreased level of mortality exhibited by the female rats at the 1.31 g/kg dose level accounted for the wide range of confidence limits.

The following clinical observations were noted in all dose groups with increasing incidence and duration with increasing dose level: diarrhea, yellow-stained abdomen, red stains around nose and mouth, ataxia, and decreased limb tone. Hypoactivity was observed in all but the 0.27 g/kg groups.

3.20 and 2.05 g/kg – Deaths occurred between days 0 and 10. No gross lesions observed at necropsy.

1.31 g/kg – Deaths occurred between days 1 and 7. Gross lesions observed in survivors were: adhesion of the stomach to liver, spleen, abdominal wall and/or cecum; cardiac thickening; and enlarged, brown spleen. No gross lesions observed in decedents.

1.05 g/kg Deaths occurred between days 3 and 9.

0.67 g/kg – Deaths occurred between days 2 and 7. One survivor had raised white areas on lung. All other survivors had no gross lesions One animal that died had gastrointestinal track distended with gas.

0.43 g/kg – One survivor had raised white areas on the lungs, all others had no gross lesions.

0.27 g/kg – Four male rats had lung abnormalities (dark red and firm and/or white focal areas). One female rat had thickened cardiac mucosa.

Conclusions

Remarks: The acute oral LD_{50} has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1B

Remarks: Reliable without restriction; comparable to guideline study.

References

Thompson, G. W. 1980. Acute Oral Toxicity – Method, Summary, Pathology with ARQUAD 2C in the Rat. RT Lab number 787409. Raltech Scientific Services, Madison, WI, U. S.

Other Available Reports

Other

Last changed: December 13, 2001
Order number for sorting: 17o1
Remarks:

5.1.1 ACUTE ORAL TOXICITY

Test Substance

Identity:	Dialkyl (octadecyl) dimethyl ammonium chloride (Quaternary ammonium compounds, di-C12-18-alkyldimethyl, chlorides; CAS RN 68391-05-9)
Purity:	69.8% in aqueous isopropanol
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	LD_{50}
GLP:	Yes
Year:	1983
Species/Strain:	Sprague Dawley rats
Sex:	Female
No. of animals per sex per dose:	Variable
Vehicle:	Undiluted
Route of administration:	Oral gavage
Remarks:	Female rats were administered the test substance using the "up and down" procedure for determination of LD_{50}. Dosages were 3846, 5000, 6500, 8450, and 10,985 mg/kg via gavage.

Results

Value:	LD_{50} = 4700 mg/kg (3500-6500 mg/kg 95% confidence interval)
Number of deaths:	3846 mg/kg .... 0/1 5000 mg/kg .... 1/2 6500 mg/kg .... 2/2 8450 mg/kg .... 3/3 10,985 mg/kg 1/1
Remarks:	Signs considered related to treatment included piloerection, hypoactivity, diarrhea, ptosis, high carriage, ataxia, chromodacryorrhea and decreased limb tone seen mainly in animals that died. Of the two surviving animals, one rat at the 5000 mg/kg dose appeared free of signs at Day 4 while the animal dosed at 3846 mg/kg appeared normal throughout the study.

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1C
Remarks:	Reliable without restriction; test procedure according to standards for the "up and down procedure".

References

Other Available Reports	Myer, J.R. 1984. Up and down procedure for estimating acute oral toxicity (LD_{50}) in rats. International Research and Development Corporation, Mattawan, MI, USA. Unpublished Report 191-1027.

Other

Last changed:	September 12, 2001
Order number for sorting:	26a
Remarks:	

5.1.1 Acute Oral Toxicity

Test Substance

Identity:	ARQUAD 2 T Ticket #16411(CAS RN 68783-78-8; Quaternary ammonium compounds, dimethylditallow alkyl, chlorides)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Regulations for the Enforcement of the Federal Hazardous Substances Act (1964)
Type:	LD_{50}
GLP:	Not stated
Year:	1980
Species/Strain:	Harlan Sprague-Dawley rat
Sex:	Male
No. of animals per sex per dose:	5
Vehicle:	None
Route of administration:	Oral gavage
Remarks:	Five male rats, 209 - 242 g at study initiation were administered the test substance by stomach tube. The test substance was administered as a 1:10 aqueous dilution at dosages of 1.00, 2.15, 4.64, 10.0 and 21.5 ml/kg body weight. Food was withheld from the rats for approximately 18 hours prior to dosing. All animals were observed closely for gross signs of systemic toxicity and mortality at frequent intervals during the day of dosages and at least once daily thereafter for a total of 14 days. At the end of the 14-day observation period the rats were weighed, sacrificed by cerebral concussion and gross necropsies were performed.

Results

Value:	$LD_{50} > 21.5$ ml/kg formulation (approx. 2.15 g/kg active substance)
Number of deaths:	0
Remarks:	All rats in the 1.00, 2.15 and 4.64 ml/kg dose levels exhibited normal behavior and appearance during the day of dosage and throughout the remainder of the study. At the 10.0 ml/kg level, all rats exhibited normal behavior and appearance during the day of dosing. On the first post-dosage day, three rats exhibited diarrhea stains and one rat exhibited serosanguineous stains around the right eye. These signs rapidly subsided and all rats generally exhibited normal appearance and behavior from day 3

through 14 of the study. The rats at the 21.5 ml/kg level exhibited depression with three rats exhibiting diarrhea or diarrhea stains on the first day of dosing. All rats exhibited diarrhea stains on the first and second day post-dose and by day 3 only one rat exhibited diarrhea stains. All rats appeared normal from day 4 through the end of the study. The average body weight gain for each group was within the normal limits for rats of this age, sex and strain. Necropsies performed at termination revealed no gross pathological alterations.

Conclusions

Remarks: The acute oral LD_{50} has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1C

Remarks: Reliable without restriction; test procedure according to national standards.

References

Young, S. M. 1975. Acute Toxicity, Irritation and Sensitization Studies of Arquad 2 T Ticket #16411. Report number 74-681-21. Hill Top Research, Inc., Cincinnati, OH, U. S.

Other Available Reports

Other

Last changed: December 13, 2001

Order number for sorting: 25a

Remarks:

5.1.1 Acute Oral Toxicity

Test Substance

Identity:	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chlorides (CAS RN 61789-80-8)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	LD_{50}
GLP:	No
Year:	1985
Species/Strain:	Harlan Fischer rat
Sex:	Male and female
No. of animals per sex per dose:	5
Vehicle:	10% hydrochloric acid
Route of administration:	Oral gavage
Remarks:	Five male and five female rats per group, 150 – 175 g (males) and 125 – 150 g (females) at study initiation were administered 500 mg/kg of the test substance by oral gavage. On the day of dosing, following dosing, the rats were observed hourly for six hours and once daily for 14 days thereafter. Mortality and overt signs of toxicity were recorded at each observation period. Mean body weights were calculated at 0, 7 and 14 days. Gross necropsy examinations were not performed.

Results

Value:	LD_{50} > 500 mg/kg
Number of deaths:	0 males, 0 females
Remarks:	Following dosing, the only sign of toxicity was generalized leg weakness, which was seen in all animals. This observation cleared by test day 2. The animals appeared normal for the remainder of the study. A mean body weight gain was observed at each time interval throughout the study.

Conclusions

Remarks:	The acute oral LD_{50} has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2B
Remarks:	Reliable with restrictions; basic data given, comparable to guidelines/standards.

References

Martin, L. D. Acute Rat Oral Study. Study number R-0-92-85. 1992. Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, U. S.

Other Available Reports

Other

Last changed:	December 13, 2001
Order number for sorting:	18
Remarks:	

5.1.1 Acute Oral Toxicity

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	Acute toxicity
GLP:	Not stated
Year:	1978 - 1979
Species/Strain:	Beagle dogs and Swiss-Webster mice
Sex:	Male and female
No. of animals per sex per dose:	3 dogs, 5 mice
Vehicle:	Sterile water
Route of administration:	Oral gavage
Remarks:	Three male and three female dogs 10 to 24 months old at study initiation were administered 432 mg/kg of the test substance by oral gavage. Five male and five female mice approximately 15 to 30 g at study initiation were administered 576 mg/kg of the test substance by oral gavage. Concentrations of both dosing solutions were 4.8% w/w. [Note: Although not specified, it was assumed that the doses were corrected to active ingredient based on consistency with data for similar test materials.] Sterile water was used in the preparation of all solutions. Prior to dosing, the dogs were fasted from food for approximately 20 - 24 hours and the mice were fasted from food for approximately 16 - 20 hours. The dogs were not fed until the day following dose administration (total fasting time approximately 40 - 48 hours). Food was returned to the mice approximately 3 - 4 hours post-dose. All animals were observed closely during the first few hours after dosing and at least twice each hour thereafter during the first working day. Animals were then observed once daily for a total of seven days. Necropsies were performed on the animals that died following dose administration.

Results

Value:	$LD_{50} > 432$ mg/kg for dogs $LD_{50} > 576$ mg/kg for mice
Number of deaths:	432 mg/kg in dogs = 0 males, 0 females 576 mg/kg in mice = 0 males, 0 females

Remarks: The test substance did not produce neurotoxic symptoms or death in mice at the highest level dosed (576 mg/kg). Because of limited solubility of the test substance, it was not feasible to dose higher levels. A single dose of 432 mg/kg administered to dogs also failed to produce neurotoxic symptoms or death.

Conclusions

Remarks: The acute oral LD_{50} has been adequately characterized. (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 2A

Remarks: Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References

Nixon, C. A., B. E. Domeyer, P. J. Reer and M. E. Volpenheim. 1981. Visible Neurotoxic Effects of a Series of Purified and Commercial Grade Quaternary Ammonium Compounds and Alkylethoxylate Nonionics Following Oral Administration to Dogs, Rabbits and Mice. Study number 1089-26077. Procter & Gamble Co., Cincinnati, OH, U. S.

Other Available Reports

Other

Last changed: December 13, 2001

Order number for sorting: 19

Remarks:

5.1.1 Acute Oral Toxicity

Test Substance

Identity:	G0610.01 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Not stated
Type:	Acute oral LD_{50} up and down procedure
GLP:	Yes
Year:	1985
Species/Strain:	Rat/Sprague-Dawley
Sex:	Male and female
No. of animals per sex per dose:	1
Vehicle:	Mineral oil
Route of administration:	Oral gavage
Remarks:	Two rats (one male and one female) per group were administered the test substance orally as a 40% w/v preparation in mineral oil at concentrations of 2.0, 2.6, 3.4, 4.4, 5.7, 7.4, 9.6, 12.5 and 16.3 g/kg. Rats were fasted for 18 to 20 hours prior to test substance administration. On the day of test substance administration, male and female rats weighed 197 to 263 g and 168 to 215 g, respectively. Rats were observed 0.5, 1, 2 and 4 hours post-dose and daily for 7 days post-dose for signs of toxicity. At the end of the 7-day observation period, rats were weighed and a gross necropsy was performed.

Results

Value:	$LD_{50} > 16.3$
Number of deaths:	0/18
Remarks:	All rats survived until study termination. Clinical observations noted in all rats during the observation period included diarrhea, rough coat, decreased motor activity and lethargy. All rats gained weight during the 7-day observation period. No visible treatment-related macroscopic lesions were noted during necropsy in any rat.

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2B
Remarks:	Reliable without restriction; comparable to guideline study.

References

Hiles, R. A. 1985. Up and Down Procedure for Estimating Acute Oral Toxicity (LD_{50}) in Rats. Study number 3029.1306. Springborn Institute for Bioresearch, Inc., Spencerville, OH, U. S.

Other

Last changed:	May 11, 2001
Order number for sorting:	37
Remarks:	

5.1.1 Acute Oral Toxicity

Test Substance

Identity:	Quaternary ammonium compounds, pentamethyltallow alkyltrimethylenedi-, dichlorides (CAS RN 68607-29-4)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	LD_{50}
GLP:	Not stated
Year:	1976
Species/Strain:	Wistar
Sex:	Male and female
No. of animals per sex per dose:	5
Vehicle:	None
Route of administration:	Oral gavage
Remarks:	Five male and five female rats per group, approximately 5 to 8 weeks old and weighing between 100 and 180 g at study initiation were administered 0.50, 0.63, 0.79, 1.00, or 1.26 ml/kg of the test substance by oral gavage at a concentration of 250 mg/ml in distilled water. This resulted in dose levels of 125, 157.5, 197.5, 250, and 315 mg/kg. The animals were fasted for 16 hours before dosing. The rats were observed at 15, 30, 60, 120 and 240 minutes after dosing and daily thereafter for 14 days. Dead animals were autopsied. All surviving animals were weighed and necropsied for gross pathology. The LD_{50} was calculated according to the method of Thompson and Weil (Biometrics. 1951. 8:51-54) at 24 hours and 14 days.

Results

Value:	LD_{50} (at 24 hours) = 250 mg/kg (95% confidence limits = 227.5 – 275 mg/kg) LD_{50} (at 14 days) = 205 mg/kg (95% confidence limits = 177.5 – 235 mg/kg)
Number of deaths:	0.50 ml/kg = 0 males, 0 females 0.63 ml/kg = 0 males, 2 females 0.79 ml/kg = 2 males, 2 females 1.00 ml/kg = 5 males, 3 females 1.26 ml/kg = 5 males, 5 females

Remarks:	All deaths occurred between 1 and 48 hours post-dosing. All surviving animals gained weight throughout the observation period. Clinical signs including abnormal gait, piloerection and decreased motor activity were observed in rats at all dose levels within the first 24 hours of dosing. One male rat in each of the 0.79, 1.0 and 1.26 ml/kg dose groups also exhibited loss of corneal reflex at one or two hours post-dose. All surviving animals appeared normal from day 2 through the end of the 14-day observation period. All animals that died or were sacrificed at the termination of the observation period showed no gross lesions at necropsy.

Conclusions

Remarks:	The acute oral LD_{50} has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References Sterner, E. and A. Stiglic. 1976. Acute Oral Toxicity in Rats, Compound: "ECM BTS 132 ETC 262". Study number 1022-18614. International Bio-Research, Inc., Zweiglabor, Hannover, Germany.

Other Available Reports

Other

Last changed:	December 13, 2001
Order number for sorting:	24
Remarks:	

5.1.2 Acute Inhalation Toxicity

Test Substance

Identity:	Arquad® 2HT-75 (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Regulations for the Enforcement of the Federal Hazardous Substances Act (1964)
Type:	LC_{50}
GLP:	Not stated
Year:	1974
Species/Strain:	Albino rats
Sex:	Male
No. of animals per sex per dose:	10
Vehicle:	Distilled water
Route of administration:	Inhalation
Remarks:	Arquad® 2HT-75 was prepared by adding one part sample to 29 parts distilled water. The rats were exposed to the test substance in an inhalation chamber for one hour. The appearance and behavior of the animals were observed continuously during the exposure period and at frequent intervals thereafter for a total of 14 days. At the end of the observation period the rats were weighed, sacrificed and gross necropsies were performed.

Results

Value:	$LC_{50} > 180.0$ mg/l of mist
Number of deaths:	0
Remarks:	The calculated chamber concentration was 180.0 mg/l of mist. Observations during the exposure period included "excited" activity upon initiation. The majority of rats exhibited preening, excessive masticatory movements, excessive salivation stains, damp hair coats, lacrimation and serosanguineous stains around the nose. Labored respiration was also noted in an occasional rat as the exposure period progressed. Upon removal from the chamber, all rats exhibited wet hair coats and marked excessive salivation and stains. Four rats exhibited serosanguineous stains around the nose and labored respiration. All rats exhibited normal appearance and behavior on the first post-exposure day and throughout the remainder of the study.

Conclusions

Remarks: Based on these results, Arquad® 2HT-75 is classified as non-toxic by inhalation exposure as this term is defined in the FHSA regulations (Author of the report). The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 2D

Remarks: Reliable with restrictions; test procedure according to national standards – only one hour exposure.

References

Young, J. A. 1974. Acute Inhalation Toxicity Study of ARQUAD® 2HT-75. Report number 74-696-21. Hill Top Research, Inc., Cincinnati, OH, U. S.

Other Available Reports

Other

Last changed: December 13, 2001

Order number for sorting: 19a

Remarks:

5.1.3 ACUTE DERMAL TOXICITY

Test Substance

Identity:	1-Hexadecanaminium, N,N,N-trimethyl-, chloride (CAS RN 112-02-7; Ammonium, hexadecyltrimethyl-, chloride)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Not stated
Type:	Acute dermal toxicity
GLP:	Not stated
Year:	1977
Species/Strain:	Rabbit/New Zealand White
Sex:	Male and female
No. of animals per sex per dose:	3
Vehicle:	None
Route of administration:	Dermal
Remarks:	Three males and three females weighed between 2.25 and 2.90 kg at study initiation. Prior to dosing, the fur was clipped from the test site (approximately 25% of the total body surface). The skin at the application site of one male and two female rabbits was abraded. The skin of the remaining rabbits was not abraded. The undiluted test substance was applied once dermally to the prepared site at the dose level of 4.3 ml/kg. The test substance was spread over the clipped area with a glass stirring rod. The entire test site was covered with two layers of 8-ply gauze, occluded with rubber dental dam and secured with porous tape. The rabbits were restrained in Newmann harnesses and returned to their cages for 24 hours. After the 24-hour exposure period, the harnesses were removed, the occlusive wraps were removed and any remaining test substance was wiped off with a wet disposable towel. Test sites were graded for signs of irritation. Each rabbit was examined thoroughly for signs of systemic toxicity, changes in behavior, mortality and dermal irritation for 14 consecutive days following the day of dosing. After the 14-day observation period, the surviving animals were weighed, killed and necropsied to observe any internal gross effects. A gross necropsy was performed on each animal that died.

Results

Value: $LD_{50} \approx 4.3$ ml/kg

Number of deaths: 2 males and 1 female.

Remarks: One female rabbit died on day 5, one male died on Day 8 and one male died on day 13. At the end of the 24-hour exposure period, all animals exhibited normal behavior and appearance. On day 3, all rabbits exhibited depressed reflexes, body cold to touch, eating and defecating very little or none at all, a clear fluid around the nose and mouth, chin and front limbs. One male and one female rabbit held their heads in a downward and tilted position and the nictitating membranes and eyelid were reddened. These signs persisted throughout the major portion of the study or until death occurred. All rabbits showed a substantial weight loss during the study. Signs of skin irritation noted at the end of the 24-hour exposure period included slight to severe erythema, moderate or severe edema and whitening of the skin of the exposure area. The erythema remained relatively unchanged throughout the study while the edema subsided slightly. Also, moderate or severe atonia was noted on day 3 through termination or until death, moderate or marked coriaceous skin from day 2 through termination or death and fissuring in three rabbits and desquamation in one animal. Necropsy findings in the animals that died included brown, liquid, fecal material around the anal area, back legs and in colon, lungs adhered to chest wall, lungs white and filled with white granular pockets, gall bladder enlarged and brownish or clear fluid around nose, mouth, chin and front limbs. No visible lesions were noted during the necropsies of the surviving animals at termination.

Conclusions

Remarks: 50% of animals died at the only dose administered. (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 2A

Remarks: Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References

Hall, R. H. Acute Percutaneous Toxicity Study in Rabbits with P0309. 1978. Project number WIL-1133-77. Wil Research Laboratories, Inc., Cincinnati, OH, U. S.

Other Available Reports

Other

Last changed: December 13, 2001

Order number for sorting: 7

Remarks:

5.1.3 Acute Dermal Toxicity

Test Substance

Identity:	Trimethyltallow alkyl, chlorides (CAS RN 8030-78-2; Quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Not stated
Type:	Acute dermal toxicity
GLP:	Not stated
Year:	1977
Species/Strain:	Rabbit/New Zealand White
Sex:	Male and female
No. of animals per sex per dose:	3
Vehicle:	None
Route of administration:	Dermal
Remarks:	Three males and three females weighing between 2.2 and 2.65 kg at study initiation. Prior to dosing, the fur was clipped from the test site (approximately 25% of the total body surface). The skin at the application site of one male and two female rabbits was abraded. The skin of the remaining rabbits was not abraded. The undiluted test substance was applied once dermally to the prepared site at the dose level of 4.0 ml/kg. The test substance was spread over the clipped area with a glass stirring rod. The entire test site was covered with two layers of 4-ply gauze, occluded with rubber dental dam and secured with porous tape. The rabbits were restrained in Newmann harnesses and returned to their cages for 24 hours. After the 24-hour exposure period, the harnesses were removed, the occlusive wraps were removed and any remaining test substance was wiped off with a wet disposable towel. Test sites were graded for signs of irritation. Because of severe toxicity observed, all rabbits were examined very closely, several times each day for signs of toxicity. The rabbits were necropsied immediately after death and gross lesions were recorded.

Results

Value:	LD_{50} < 4.0 ml/kg (100% mortality at the only dose administered)
Number of deaths:	3 male and 3 female.

Remarks: The acute oral dose of the test substance produced toxicity in all six rabbits that was similar in nature. All rabbits died between Days 3 and 8 following dosing. The toxicity signs prior to death appeared to be related to central nervous system effects and there was no difference in the response of males and females or between rabbits with abraded or unabraded skin. Clinical observations were; unable to hold head up, unable to hold ears erect, increased respiration rate, increased heart rate, ataxia, depression, excessive salivation, reduced motor reflexes, reduction or lack of food consumption and defecation, and hyperexcitable when handled. These signs continued until death. Moderate to severe skin irritation was observed in all rabbits following the single application. Gross lesions observed at necropsy included dilation of blood vessels in the skin, gastrointestinal tract and the surface of the brain in all rabbits. The renal blood vessels and posterior vena cava were enlarged in all but one rabbit. The pituitary was dark red to purple in color in rabbits in which the pituitary was observed (one male and one female).

Conclusions

Remarks: 100% mortality at the only dose administered, i.e. 4.0 ml/kg.
(American Chemical Council Fatty Nitrogen Derivatives Panel, Cationic Task Group).

Data Quality

Reliability (Klimisch): 2A

Remarks: Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References

Hall, R. H. Acute Percutaneous Toxicity Study in Rabbits with P7256. 1978. Project number WIL-1098-77. Wil Research Laboratories, Inc., Cincinnati, OH, U. S.

Other Available Reports

Other

Last changed: December 13, 2001

Order number for sorting: 15

Remarks:

5.1.3 ACUTE DERMAL TOXICITY

Test Substance

Identity:	Trimethyltallow alkyl, chlorides (CAS RN 8030-78-2; Quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Not stated
Type:	Acute dermal toxicity
GLP:	Not stated
Year:	1977
Species/Strain:	Rabbit/New Zealand White
Sex:	Male and female
No. of animals per sex per dose:	3
Vehicle:	None
Route of administration:	Dermal
Remarks:	Three males and three females weighed between 2.35 and 2.60 kg at study initiation. Prior to dosing, the fur was clipped from the test site (approximately 25% of the total body surface). The skin at the application site of one male and two female rabbits was abraded. The skin of the remaining rabbits was not abraded. The undiluted test substance was applied once dermally to the prepared site at the dose level of 4.7 ml/kg. The test substance was spread over the clipped area with a glass stirring rod. The entire test site was covered with 8-ply gauze, occluded with rubber dental dam and secured with porous tape. The rabbits were restrained in Newmann harnesses and returned to their cages for 24 hours. After the 24-hour exposure period, the harnesses were removed, the occlusive wraps were removed and any remaining test substance was wiped off with a wet disposable towel. Test sites were graded for signs of irritation. Each surviving rabbit was examined thoroughly for signs of systemic toxicity, changes in behavior, mortality and dermal irritation for 14 consecutive days following the day of dosing. After the 14-day observation period, the surviving rabbit was weighed, killed, and necropsied to observe any internal gross effects. A gross necropsy was performed on each animal that died.

Results

Value: LD_{50} < 4.7 ml/kg (5 of 6 animals died at the only dose administered).

Number of deaths: 2 male and 3 female

Remarks: There were no remarkable differences between the rabbits with abraded or unabraded skin. Three rabbits (one male and two females) died during the 24-hour exposure period. One female rabbit died on Day 6 and one male rabbit died on day 11 post-dosing. No signs of systemic toxicity were observed prior to death for the animals that died during the 24-hour exposure period. At the end of the 24-hour exposure, the three surviving animals showed depressed reflexes, cold and drooping ears, and intermittent tremors. One rabbit also exhibited hunched posture. These signs persisted until death in two of the animals. Wet fur around the mouth, side of head and front paws was noted in one rabbit on day 3 and persisted until its death on day 11. As for the surviving animal, signs of toxicity persisted for five days after which the animal began eating, defecating, and exhibiting normal behavior and appearance until termination. The surviving animal and the animals that died after the 24-hour exposure period showed substantial weight loss. Skin irritation noted in the three surviving animals at the end of the 24-hour exposure period included slight to moderate erythema, edema and atonia. One animal exhibited slight coriaceous skin. By day 2, the edema and atonia increased to severe and all rabbits exhibited marked coriaceous skin. These signs persisted to death or termination of the animals. The necropsy of one rabbit that died during the 24-hour exposure revealed gas-filled and distended large intestines, stomach wall very thin and lungs red and adhered to the chest wall. No gross lesions were observed in the other two rabbits that died during the exposure period. White mucoid substance in mouth, intestines irritated and thin stomach wall were observed during the necropsy of one rabbit that died on day 6. The one rabbit that died on day 11 had right lung lobes dark red and red intestines at necropsy. The necropsy of the surviving animal revealed clear fluid in the abdominal cavity and body fat stores depleted.

Conclusions

Remarks: 5 of 6 animals died at the only dose administered. (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References

Hall, R. H. Acute Percutaneous Toxicity Study in Rabbits with P0306. 1978. Project number WIL-1137-77. Wil Research Laboratories, Inc., Cincinnati, OH, U. S.

Other Available Reports

Other

Last changed:	December 13, 2001
Order number for sorting:	16
Remarks:	

5.1.3 ACUTE DERMAL TOXICITY

Test Substance

Identity:	G0610.01 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	85%
Remarks:	

Method

Method/guideline followed:	Not stated
Type:	LD_{50}
GLP:	Yes
Year:	1985
Species/Strain:	Rabbit/New Zealand Albino
Sex:	Male and female
No. of animals per sex per dose:	3
Vehicle:	None
Route of administration:	Dermal
Remarks:	Three male and three female rabbits, weighing 2466 to 2858 g, were administered a single dose of the test substance dermally at a level of 2000 mg/kg. The test substance was used as received. Rabbits were clipped free of hair. The skin of one male and two females was abraded. The skin of the remaining two males and one female was left intact. After test substance application, the trunk of each rabbit was encased with an occlusive dressing for 24 hours. Following the 24-hour exposure period, the dressing was removed and the skin sites cleansed. All rabbits were observed daily thereafter for 14 days for mortality, skin response and general behavior. At the end of the 14-day observation period, the rabbits were sacrificed and subjected to a gross necropsy.

Results

Value:	> 2000 mg/kg
Number of deaths:	0/6
Remarks:	All rabbits survived. The test substance produced severe erythema, moderate edema and moderate atonia in all six rabbits during the observation period. Slight desquamation (3/6), moderate fissuring (2/6), and eschar and exfoliation (4/6) also was observed during the observation period. At study termination, skin reactions consisted of slight to moderate erythema (5/6) and eschar with exfoliation (1/6). Body weight gain was noted for all rabbits. Necropsy examinations revealed minimal to slight erythema (4/6) and moderate exfoliation and eschar (1/6) in association with

the dorsal area of treated skin and were considered to be treatment-related. There were no other significant lesions noted.

Conclusions

Remarks: The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1B

Remarks: Reliable without restriction; comparable to guideline study.

References

Nixon, G. A. 1985. Acute Percutaneous Toxicity. Study number B85-0374. The Proctor and Gamble Company, Cincinnati, OH, U. S.

Other

Last changed: May 11, 2001

Order number for sorting: 27

Remarks:

5.4 REPEATED DOSE TOXICITY

Test Substance

Identity:	P0389 (CAS RN 112-02-7; Ammonium, hexadecyltrimethyl-, chloride)
Purity:	54.5% in aqueous isopropanol
Remarks:	

Method

Method/Guideline followed:	Not stated
Test type:	Dermal
GLP:	Yes
Year:	1978
Species:	Rabbit
Strain:	New Zealand White
Route of administration:	Dermal
Duration of test:	28 days
Doses/concentration levels:	0.5% (w/v): 2.0 ml/kg (10 mg/kg/day)
Sex:	Male and female
Exposure period:	4 weeks
Frequency of treatment:	5 days/week
Control group and treatment:	Yes, distilled water
Postexposure observation period:	None
Statistical methods:	Body weight, organ weight and hematology data were compared by analysis, Bartlett's test for homogeneity of variance and the least significant differences test.
Remarks:	Five rabbits/sex/group were treated cutaneously with the test chemical for 5 days/week for 4 weeks at a dose of 0 or 10 mg/kg/day (0, 0.5% aqueous solutions, respectively). Dosage volume was 2.0 ml/kg body weight with an approximate 6.5- to 7-hour exposure period. As needed throughout the study, approximately 25% of the body area hair was clipped. The skin of all rabbits was abraded with a clipper head prior to each application. The animals were restrained with collars during the exposure period. Following the exposure period, the animals were washed with water. All rabbits were examined daily for pharmacotoxic signs and mortality. Dermal irritation readings were recorded daily. The animals were weighed weekly during the exposure period. Blood was collected for hematology measurements before initiation of dosing and prior to termination. Liver and kidneys were weighed at necropsy. A full list of tissues was collected for histopathological evaluation.

Results

NOAEL (NOEL):	10 mg/kg/day (except for skin irritation)
LOAEL (LOEL):	Not applicable
Actual dose received:	As applied
Toxic response/effects:	Skin irritation only
Statistical results:	See below
Remarks:	Two control group animals died during the study. Erythema was the only sign of dermal irritation noted in all rabbits in the test group. The very slight or slight erythema initially appeared on study days 4 to 8 and for most rabbits the erythema became slight to moderate before subsiding. After study day 17, there was no indication of erythema for four treated rabbits and very slight/slight atonia, desquamation and coriaceousness were observed in the other animals. For most treated rabbits, very slight or slight fissuring was noted but was not evident after study day 17. There were no treatment-related effects on body weight, hematology, organ weight, gross necropsy findings or histopathology (except for treated areas of the skin).

Conclusions

Remarks:	The endpoint has been adequately characterized (Chemical Manufacturer's Association Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented study report which meets basic scientific principles

References

Spicer, E.J.F. 1979. Subchronic percutaneous toxicity (twenty-eight days) in rabbits. International Research and Development Corporation, Mattawan, MI, USA. Unpublished report #191-217 (a)

Other

Last changed:	September 12, 2001
Order number for sorting:	7aa
Remarks:	

5.4 Repeated Dose Toxicity

Test Substance

Identity:	G0123.02 (CAS RN 68391-05-9; Quaternary ammonium compounds, di-C12-18-alkyldimethyl, chlorides)
Purity:	69.8% in aqueous isopropanol
Remarks:	

Method

Method/Guideline followed:	Not stated
Test type:	Dermal
GLP:	Yes
Year:	1984
Species:	Rabbit
Strain:	New Zealand White
Route of administration:	Dermal
Duration of test:	28 or 91 days
Doses/concentration levels:	0.5% (w/v): 2.0 ml/kg (10 mg/kg/day)
Sex:	Male and female
Exposure period:	4 or 13 weeks
Frequency of treatment:	5 days/week
Control group and treatment:	Yes, deionized water
Postexposure observation period:	None
Statistical methods:	Body weight, organ weight and hematology data analyzed using the F-test for equality of variance and either the t-test (equal variance) or the Wilcoxon Rank Sum Test.
Remarks:	Three rabbits/sex/group (28-days) or 5 rabbits/sex/group (91-days) were treated cutaneously with the test chemical for 5 days/week at a dose of 0 or 10 mg/kg/day (0, 0.5% aqueous solutions, respectively). Dosage volume was 2.0 ml/kg body weight with an approximate 4-hour exposure period. Prior to the first dose and as needed throughout the study, the hair was clipped from the back from shoulder to rump, approximately 15 cm wide. Approximately 25% of the total body surface was covered. The animals were restrained with collars during the exposure period. Following the 4-hour exposure, the animals were washed with water. All rabbits were examined daily for pharmacotoxic signs and mortality. Daily dermal irritation readings, according to the method of Draize, were read immediately prior to dosing. The animals were weighed weekly during the exposure period. Blood was collected for hematology measurements before initiation of dosing and prior to termination (at 28 or 91 days). Liver and kidneys were weighed at necropsy. A full list of tissues was collected for histopathological evaluation.

Results

NOAEL (NOEL):	10 mg/kg/day (except for skin irritation)
LOAEL (LOEL):	Not applicable
Actual dose received:	As applied
Toxic response/effects:	Skin irritation only
Statistical results:	See below
Remarks:	No dermal irritation was observed in the control group. The highest incidence and most severe dermal irritation noted in the test group occurred during the second week of study. The irritation included moderate degrees of erythema, edema, atonia, desquamation and fissuring. After week 3, all rabbits had little irritation; however a low incidence of erythema and desquamation was occasionally observed. There were no treatment-related effects on body weight, hematology, organ weight, gross necropsy findings or histopathology

Conclusions

Remarks:	The endpoint has been adequately characterized (Chemical Manufacturer's Association Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented study report which meets basic scientific principles

References

Johnson, D.E. 1986. 28-day/91-day subchronic percutaneous toxicity with G0123.02. International Research and Development Corporation, Mattawan, MI, USA. Unpublished report #191-1026

Other

Last changed:	September 13, 2001
Order number for sorting:	26b
Remarks:	

5.4 Repeated Dose Toxicity

Test Substance

Identity:	Dimethyl-di-"Hydrogenated Tallow" Ammonium Chloride (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Test type:	Oral feed
GLP:	No
Year:	1971
Species:	Dog
Strain:	Beagle
Route of administration:	Dietary
Duration of test:	90-day
Doses/concentration levels:	14, 140 and 2800 ppm (approximately 0.5, 5, 100 mg/kg/d)
Sex:	Male and female
Exposure period:	90-days
Frequency of treatment:	Treated and control diets were available for 3 hours per day, seven days per week.
Control group and treatment:	Yes, laboratory diet alone
Postexposure observation period:	None
Statistical methods:	None performed
Remarks:	Eight purebred beagle dogs (four male and four female) were assigned to three treatment and one control group. Animals were group housed by sex and dose group. The test substance was incorporated into a stock diet and made available to the dogs three hours per day, seven days a week for 90-days. The control group received the stock diet at the same frequency. At the end of each seven-day period, all unconsumed food was collected and weighed. Food consumption was then calculated and recorded. Body weights were recorded initially then weekly for the duration of the test. The animals were observed daily for clinical signs or symptoms indicative of systemic toxicity. Hematology, blood chemistry and urinalysis parameters were evaluated in all dogs just prior to test initiation and after 45 and 90 days of testing:

At the conclusion of the investigation the dogs were sacrificed and a gross necropsy evaluation was performed. All major tissues and organs were examined grossly. The weights of the following organs were obtained: liver, kidneys, heart, brain, spleen, gonads, adrenal glands, thyroid gland and pituitary gland. Histopathologic examination were performed on selected tissues from all animals.

Results

NOAEL (NOEL):	> 2800 ppm (approximately 100 mg/kg/d)
LOAEL (LOEL):	None
Actual dose received:	Not stated
Toxic response/effects:	None
Statistical results:	None performed
Remarks:	No fatalities occurred during the study. Body weight, body weight gains and food consumption were comparable across all groups. There were no treatment related effects noted in urinalysis or hematologic parameters evaluated. A comparison of baseline, 45- and 90-day data revealed no intergroup differences with respect to the blood chemistry parameters evaluated. One male dog receiving 2800 ppm displayed an elevated absolute and relative (to body weight) liver weight. Since this was an isolated incidence and all other test animals displayed normal absolute and relative liver weights, this was not considered related to test material consumption. Also, there were no gross or microscopic lesions observed in the liver of this animal. No other differences in organ weights were noted between dogs in the test and control groups. There were no treatment-related effects noted in the gross or microscopic evaluations. Calcium-like deposits were noted in the lumen of some stomach glands of one low level male dog. Since this was a single incident and did not appear in the higher dose levels it was not considered related to treatment.

Conclusions

Remarks:	Reproductive organs weighed and examined microscopically adequate for SIDS reproductive screening. The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References Lindberg, D. C. and P. L. Wright. 1971. 90-Day Subacute Oral Toxicology Study with Dimethyl-di-“Hydrogenated Tallow” Ammonium Chloride in Beagle Dogs. 1971. IBT number C8934. Industrial Bio-Test Laboratories, Inc., Northbrook, IL, U. S.

Other

Last changed:	December 13, 2001
Order number for sorting:	20b
Remarks:	

5.4 Repeated Dose Toxicity

Test Substance

Identity:	B0278-01 (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)
Purity:	78.2% in water/isopropanol (9%/13%)
Remarks:	

Method

Method/Guideline followed:	Not stated
Test type:	Dermal
GLP:	Yes
Year:	1980
Species:	Rabbit
Strain:	New Zealand White
Route of administration:	Dermal
Duration of test:	91 days
Doses/concentration levels:	140 or 10 mg/kg/day
Sex:	Male and female
Exposure period:	91 days
Frequency of treatment:	5 days/week
Control group and treatment:	Yes, distilled water
Postexposure observation period:	None
Statistical methods:	Differences were analyzed within each sex using a one-way Analysis of Variance followed by Dunnett's test where significant ($p \leq .05$) differences were indicated among treatment groups in the analysis of Variance.
Remarks:	Range-Finding Study: Two males and two females/group were treated cutaneously with the test chemical for 5 days/week for 2 weeks at doses of 0, 20, 60, 100 and 140 mg/kg/day (0, 1, 3, 5 and 7% aqueous solutions, respectively). Dosage volume was 2.0 ml/kg body weight with an approximate 6-hour exposure period. All rabbits were examined daily for pharmacotoxic signs and mortality. Daily dermal irritation readings, according to the method of Draize, were read immediately prior to the next application of the test substance. The animals were weighed at initiation, once weekly to adjust the dosages, and at termination. Definitive Study: Five animals/sex/group were treated with the test solutions 6 hours/day, 5 days/week for 13 weeks. Just prior to the first dose and as needed throughout the study, the hair was clipped from the back from shoulder to rump, approximately 10 cm wide. The test substance was

applied through a syringe onto the back and, with gentle inunction using a glass rod, spread evenly over the test site. The animals were restrained with collars during the exposure period. Following the 6-hour exposure, the animals were washed with water. Animals were examined daily for gross pharmacotoxic signs and mortality. Daily dermal irritation readings, according to the method of Draize, were read immediately prior to the next application of the test substance. The animals were weighed at initiation, once weekly to adjust the dosages, and at termination. Blood was collected for hematology measurements before initiation of dosing and prior to termination. Liver and kidneys were weighed at necropsy. A full list of tissues was collected for histopathological evaluation.

Results

NOAEL (NOEL): 140 mg/kg/day (except for skin irritation)
LOAEL (LOEL): Not applicable
Actual dose received: As applied
Toxic response/effects: Skin irritation only
Statistical results: See below
Remarks: Range-Finding Study: Based upon changes in animal body weights and the severity of skin reactions, a high dose level of 140 mg/kg of test solution (7% w/v) was selected for the definitive study.

Definitive Study: No dermal irritation was noted in control animals although three of the animals were observed with soft stools, diarrhea and purulent ocular discharge occasionally during the study. Slight to severe erythema and edema with associated skin changes were observed in the 140 mg/kg/day group during the first 2 weeks of the study. Over the next two weeks, these findings subsided and during the last 9 weeks of the study, only slight erythema, edema, desquamation and fissuring were consistently observed. In the 10 mg/kg/day group, slight erythema was observed frequently during the first four weeks of the study and only occasionally thereafter. Soft stool and diarrhea were observed in treated animals similar to the controls. There were no treatment-related effects on body weight, hematology, organ weight, gross necropsy findings or histopathology.

Conclusions

Remarks: The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 2A

Remarks: Reliable with restrictions; acceptable, well-documented study report which meets basic scientific principles

References

Anderson, D.D. 1981. Raltech Scientific Services, Madison, Wisconsin, USA. Subchronic 91-day percutaneous toxicity study of B0278-01 in rabbits. Unpublished report #792093

Other

Last changed: September 13, 2001

Order number for sorting: 20b3

Remarks:

5.4 REPEATED DOSE TOXICITY

Test Substance

Identity:	UDL-1017 (CAS RN 61789-81-9; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, Me sulfates)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	
Test type:	Oral feed
GLP:	No
Year:	1976
Species:	Rat
Strain:	CD Sprague-Dawley
Route of administration:	Dietary
Duration of test:	153 to 154 Days
Doses/concentration levels:	0.25, 0.5 and 10% in the diet (approximately 170, 365, and 750 mg/kg/day)
Sex:	Male and female
Exposure period:	153 to 154 Days
Frequency of treatment:	Treated and control diets were available continuously in the diet, seven days per week.
Control group and treatment:	Yes, laboratory diet alone
Postexposure observation period:	None
Statistical methods:	Body weight, food consumption, organ weights, and organ to body weight ratios were compared to control using Dunnett's test. Hematology and clinical chemistry parameters were compared to the control by the F-test and Student's t-test. When variances differed significantly (F-test), Student's t-test was appropriately modified and Cochran's approximation used. Mean values of all dose groups were compared to those of the control group at each time interval.
Remarks:	Groups of forty rats (20 males and 20 females) were administered the test substance orally at concentrations of 0.25, 0.5 and 10% in the diet. Rats were offered the diet continuously. Initially, the study was scheduled to be run for 13 weeks; however, after evaluation of the 13-week necropsy data revealed evidence of compound-related lesions, the remaining rats were dosed an additional nine weeks. Appropriate amounts of the test substance were mixed with Mazola® Corn Oil and incorporated into standard laboratory diet weekly. Upon arrival at the laboratory, rats were four to five weeks old. Just prior to

treatment, body weight ranges for males and females were 98 to 160 g and 107 to 151 g, respectively. Rats were observed daily for physical appearance, signs of local or systemic toxicity, pharmacologic effects or mortality. Ophthalmoscopic examinations were conducted pretest and in week 13. Body weights were taken twice pretest, weekly during treatment and at terminal sacrifice (after fasting). Food consumption was recorded weekly beginning one week prior to treatment. During weeks 4 and 13, five rats/sex/group were randomly selected for hematology (hemoglobin; hematocrit; erythrocytes; total and differential leukocytes; erythrocyte morphology; and mean corpuscular volume, hemoglobin and hemoglobin concentration) and clinical chemistry (serum glutamic pyruvic transaminase; alkaline phosphatase; blood urea nitrogen; fasting glucose; total protein; albumin; globulin; and A/G ratio) evaluations. During week 13, five rats/sex/group were randomly selected for urinalysis (gross appearance; protein; glucose; pH; specific gravity; ketones; bilirubin; and occult blood) evaluations. Forty rats (five/sex/group) during week 4 (34 days of treatment), 60 rats (ten/sex for control and high groups and five/sex for remaining two groups) during week 13, and 60 rats (five/sex for control and high groups and ten/sex for remaining two groups) during week 22 were sacrificed and necropsies conducted. The following organs were weighed and organ/body weight ratios calculated: pituitary, adrenals, gonads, heart, kidneys and liver. The following tissues were preserved from all animals and examined histopathologically for the control and high dose groups (five/sex at 4 weeks and 22 weeks and ten/sex at 13 weeks): adrenals, bone (rib junction), bone marrow (sternum), brain (two sections with meninges), esophagus, eye (with optic nerve), gonad (testis, epididymis, ovary, oviduct), heart (with coronary vessels), intestine (cecum, colon, duodenum, ileum, jejunum), kidney, liver, lung, lymph node (mesenteric, pulmonary), mammary gland, pancreas, pituitary, prostate (ventral), salivary gland, seminal vesicle, skin, spleen, stomach, thyroid, tongue, trachea, urethra, ureters, urinary bladder, uterus (cervix and vagina), tissue masses and gross lesions.

Results

NOAEL (NOEL):	None established
LOAEL (LOEL):	0.25% in diet; approximately 170 mg/kg/day
Actual dose received:	Approximately 170, 365, or 750 mg/kg/day

Toxic response/effects:	See below
Statistical results:	See below
Remarks:	All animals survived the duration of treatment. Clinical signs and ophthalmoscopic examinations did not reveal any abnormalities considered to be treatment-related. An initial decrease in weight gain was noted in the high dose group. The majority of absolute weight, however, was within 10% of the control weights. Elevations in the mean serum glutamic pyruvic transaminase (SGPT) values were noted in the mid and high dose males and females at thirteen weeks. The albumin (ALB) values and the albumin/globulin ratios (A/G) of the high dose males also were greater than those of control at 13 weeks. When compared with the control, the mean absolute and relative (to body weight) adrenal weights were greater in all test substance-treated groups of females and in the mid and high dose groups of males. The absolute and relative liver weights of all test substance-treated groups of females also were elevated. No remarkable differences from control were noted in the liver weights or ratios of the test substance-treated males. Microscopic treatment-related changes were observed in tissues from rats of all test substance-treated groups necropsied at all intervals of the experiment. The treatment-associated changes were observed in the mesenteric and pulmonary lymph nodes, adrenal glands and liver. Generally, the lymph node changes were the earliest treatment-related change (i.e. following 34 days of treatment) and the only change with a notable gross manifestation. The incidence of all treatment-related microscopic changes were similar in rats of all groups necropsied after 13 weeks and 22 weeks of treatment with the test substance. Reproductive organs were examined, meeting the requirements for SIDS/HPV reproductive screening.

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study.

References Killeen, J. C., Jr. and W. E. Rinehart. 1976. A Subchronic Oral Toxicity Study of UDL-1017 in Rats. Project number 75-1219. Bio/dynamics, Inc.

Other

Last changed: December 13, 2001

Order number for sorting: 22b

Remarks:

5.4 Repeated Dose Toxicity

Test Substance

Identity:	Arquad 3.16 (CAS RN 52467-63-7; Tricetylmethyl ammonium chloride)
Purity:	86.0 %
Remarks:	

Method

Method/guideline followed:	Sixth amendment (79/831/EEC-1979) to the European Community Directive 67/548/EEC
Test type:	Oral
GLP:	Yes
Year:	1990
Species:	Rat
Strain:	Sprague-Dawley CD
Route of administration:	Oral feeding
Duration of test:	28 Days
Doses/concentration levels:	0, 40, 200 and 1000 mg/kg/day
Sex:	Male and female
Exposure period:	28 Days
Frequency of treatment:	Continuous
Control group and treatment:	Yes, concurrent, untreated diet
Postexposure observation period:	None
Statistical methods:	Student's t-test, Dunnett's test or Fisher's exact probability test.
Remarks:	Groups of rats (six males and six females) were administered the test substance continuously in the diet for 28 days at concentrations of 40, 200 and 1000 mg/kg/day. A group of control rats (six males and six females) received untreated diet of the same batch at the same frequency as treated rats. Animals were group housed by sex and dose group, six per cage. Rats were 28 to 35 days old at study initiation. Males and females weighed 102 to 143 and 95 to 122 grams, respectively, at study initiation. Rats were observed twice daily throughout the treatment period for evidence of reaction to treatment or ill health. A detailed weekly examination was conducted, including palpation. Food consumption was calculated weekly for each group. Body weights were recorded on the day that treatment commenced, at twice weekly intervals during the treatment period and immediately before necropsy. On Day 28 of treatment, prior to sacrifice, blood samples were withdrawn from the retro-orbital sinus of each rat after overnight fasting. The following parameters were examined from these blood samples: packed cell volume, hemoglobin

concentration, erythrocyte count, mean cell hemoglobin concentration, mean cell volume, mean cell hemoglobin and total and differential leukocyte count. In addition, the following blood chemistry parameters were evaluated: alkaline phosphatase activity, alanine amino-transferase activity, aspartate amino-transferase activity, urea concentration, glucose concentration, total bilirubin concentration, creatinine concentration, total protein concentration, electrophoretic protein fractions and sodium, potassium, chloride, calcium and inorganic phosphorus concentrations. At the end of the 28-day treatment period, all rats were sacrificed and subjected to a detailed necropsy. The following organs were weighed: adrenals, kidneys, heart, spleen, testes and liver. The following tissues were examined microscopically: adrenals, kidneys, heart, spleen, lymph node (mesenteric) and liver.

Range-finding study

Groups of rats (three males and three females) were administered the test substance continuously in the diet for 14 days at concentrations of 500, 2500, 5000 and 10000 ppm. A group of control rats (three males and three females) received untreated diet of the same batch at the same frequency as treated rats. Animals were group housed by sex and dose group, three per cage. Rats were approximately four to five weeks old at study initiation. Males and females weighed 99 to 135 and 100 to 121 grams, respectively, at study initiation. Rats were observed twice daily throughout the treatment period for evidence of reaction to treatment or ill health. A detailed weekly examination was conducted, including palpation. Food consumption was calculated weekly for each group. Body weights were recorded on the day that treatment commenced, at twice weekly intervals during the treatment period and immediately before necropsy. At the end of the 14-day treatment period, all rats were sacrificed and subjected to a detailed necropsy. The following organs were weighed: adrenals, kidneys and liver.

Results

NOAEL (NOEL):	40 mg/kg/day
LOAEL (LOEL):	200 mg/kg/day
Actual dose received:	39.9, 198.3 and 1007 mg/kg/day for males 39.1, 206.5 and 1045 mg/kg/day for females
Toxic response/effects:	Described below
Statistical results:	Described below

Remarks:

All rats survived until scheduled sacrifice and no signs of reaction to treatment were observed during the treatment period. Food consumption, body weight gains and food utilization (amount of food consumed per unit of bodyweight gain) were unaffected by treatment. Results of the hematology did not reveal any treatment-related effects. Blood chemistry examination revealed a slight increase in alanine amino-transferase activity in animals receiving 1000 mg/kg/day when compared with controls. Organ weight analysis and macroscopic pathology did not reveal any treatment-related effects. Histologic evaluations revealed statistically significant increases in histiocytic hyperplasia in the mesenteric lymph nodes in male and female rats receiving 1000 mg/kg/day. A few animals from the 200 mg/kg day dosage group also were affected: however, the group incidence was not statistically significantly different from the control.

<u>Range-finding study</u>
The actual doses received were 70.86, 386.9, 764.4 and 1470 mg/kg/day for the males and 71.45, 348.2, 674.2 and 1347 mg/kg/day. All rats survived until scheduled sacrifice and no signs of reaction to treatment were observed during the treatment period. Food consumption, body weight gains and food conversion ratios were unaffected by treatment. Organ weight analysis did not reveal any changes related to treatment with the test substance. Macroscopic pathology findings were unremarkable. It was concluded that administration of the test substance at dietary concentrations of 500, 2500, 5000 or 10000 ppm did not produce any evidence of toxicity. Based on the results from this study, doses of 40, 200 and 1000 mg/kg/day were selected for the four-week dietary study.

Conclusions

Remarks:

It was concluded that dietary administration of the test substance at concentrations designed to achieve dosages of 40, 200 and 1000 mg/kg/day produced minimal evidence of toxicity. (Author of report)
The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report that meets basic scientific principles.

References

Vandaele, E. A. N. 1990. Arquad 3.16: Four-Week Toxicity Study By Dietary Administration to Rats. Report number 90/AKL010b/0492. Life Science Research Limited, Suffolk, UK.

Vandaele, E. A. N. 1990. Arquad 3.16: 14-Day Toxicity Study By Dietary Administration to Rats. Report number 90/AKL010a/0351. Life Science Research Limited, Suffolk, UK.

Other

Last changed:	May 29, 2001
Order number for sorting:	38 and 39
Remarks:	

5.5 Genetic Toxicity *In vitro*

Test Substance

Identity:	P1232 (CAS RN 112-00-5; Ammonium, dodecyltrimethyl-, chloride)
Purity:	24.7% aqueous solution
Remarks:	

Method

Method/Guideline followed:	Ames, B. N. 1975. Mut. Res. 31:347.
Type:	Reverse mutation assay
System of testing:	Bacterial
GLP:	Yes
Year:	1982
Species/Strain:	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537 and TA1538
Metabolic activation:	With and without S9 activation
Concentrations tested:	0.004 – 0.4 µl per plate
Statistical methods:	None
Remarks:	The test was run in triplicate and a three-fold increase in back mutations was considered as the criterion for a positive test for mutagenicity. Plate incorporation assay was used. Vehicle used was dimethylsulphoxide.

Results

Result:	Negative with and without metabolic activation
Cytotoxic concentration:	0.1 µl/plate
Genotoxic effects:	Negative with and without metabolic activation
Statistical results:	None
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized (Chemical Manufacturer's Association Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2C
Remarks:	Reliable with restrictions; comparable to guideline study with acceptable restrictions.

References

Haworth, S.R. 1982. Salmonella/Mammalian-microsome mutagenesis assay (Ames test). Microbiological Associates, Bethesda, MD, USA. Unpublished report T1806.501.

Other

Last changed: September 12, 2001
Order number for sorting: 2c3a
Remarks:

5.5 GENETIC TOXICITY *IN VITRO*

Test Substance

Identity:	P1232 (CAS RN 112-00-5; Ammonium, dodecyltrimethyl-, chloride).
Purity:	24.7% aqueous solution
Remarks:	

Method

Method/guideline followed:	Not stated
Type:	Mammalian cell forward mutation assay
System of testing:	Nonbacterial
GLP:	Yes
Year:	1982
Species/Strain:	L5178Y/TK+/- mouse lymphoma cells
Metabolic activation:	With and without S-9 activation
Concentrations tested:	0.0038 to 0.050 µl/ml (10 concentrations) without S9 0.012 to 0.16 µl/ml (10 concentrations) with S9
Statistical methods:	Not stated.
Remarks:	The test article was tested in the L5178Y TK+/- Mouse Lymphoma Mutagenesis assay in the presence and absence of rat liver S-9. A preliminary cytotoxicity assay was performed (0.001 to 100 µl/ml). The cells were exposed to the test chemical, positive control and negative control for 4 hours. An expression time of 2 days was allowed with cell population adjustment at 24 and 48 hours. At the end of the expression period, the cells were placed in cloning medium. Cell counts were made for each preparation and the appropriate number of cells were removed and plated. Total number of colonies per plate and the mutation frequency were determined . The criteria for a positive test were: if there was a positive dose response and one or more of the three highest doses exhibited a mutant frequency which was two-fold greater than the background level. A two-fold increase without dose response was considered equivocal and the test was considered negative if no cultures exhibited a two-fold increase in mutant frequency.

Results

Result:	None of the treated cultures that were cloned exhibited a significant increase in mutant frequency over the average mutant frequency of the solvent controls. There was no evidence of a dose response. The results indicate that the test article is negative in this assay.

Cytotoxic concentration:	0.01 µl/ml without metabolic activation 0.1 µl/ml with metabolic activation
Genotoxic effects:	Negative with and without metabolic activation
Statistical results:	None
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study.

References

Kirby, P.E. 1982. Test for chemical induction of mutation in mammalian cells in culture; the L5178Y TK+/- mouse lymphoma assay. Microbiological Associates, Bethesda, MD, USA. Unpublished report, study number T1806.701.

Other

Last changed:	September 11, 2001
Order number for sorting:	2c3
Remarks:	

5.5 GENETIC TOXICITY *IN VITRO*

Test Substance

Identity:	Ammonium, dodecyltrimethyl-, chloride (CAS RN 112-00-5).
Purity:	24.7% aqueous solution
Remarks:	

Method

Method/Guideline followed:	None
Type:	Unscheduled DNA synthesis assay (UDS)
System of testing:	Nonbacterial
GLP:	Yes
Year:	1982
Species/Strain:	Rat primary hepatocyte
Metabolic activation:	None
Concentrations tested:	Ranging from 0.004 to 0.1 µl/ml
Statistical methods:	None
Remarks:	A preliminary assessment of toxicity was conducted to select dose levels for the UDS assay. For the UDS assay, male rat hepatocytes were treated with the test substance at concentrations ranging from 0.004 µl/ml to 0.1 µl/ml. The positive control was dimethyl benzanthrazene (DMBA).

Results

Result:	Concentrations below 0.048 µl/ml were nontoxic. Eight treatments ranging from 0.004 µl/ml to 0.048 µl/ml were selected for analysis of nuclear labeling. No indication of induction of UDS by the test substance was observed. Negative and positive controls had nuclear grain counts in the acceptable range.
Cytotoxic concentration:	Lethal at concentrations exceeding 0.048 µl/ml
Genotoxic effects:	Inactive
Statistical results:	None
Remarks:	None

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1B
Remarks:	Reliable without restriction; comparable to guideline study.

References	Coppinger, W. J. 1983. Unscheduled DNA synthesis assay in primary cultures of rat hepatocytes. Procter & Gamble Co., Cincinnati, OH, USA. Unpublished report M0020.

Other

Last changed:	September 11, 2001
Order number for sorting:	2c2
Remarks:	

5.5 GENETIC TOXICITY *IN VITRO*

Test Substance

Identity:	Cetyltrimethylammonium chloride (CAS RN 112-02-7; Ammonium, hexadecyltrimethyl-, chloride)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	Reverse mutation assay
System of testing:	Bacterial
GLP:	Yes
Year:	1983
Species/Strain:	*Salmonella typhimurium* TA98 and TA100
Metabolic activation:	With and without S9 activation
Concentrations tested:	Not stated
Statistical methods:	None
Remarks:	Pre-incubation assay

Results

Result:	Negative
Cytotoxic concentration:	Not stated
Genotoxic effects:	None
Statistical results:	None
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions; peer review article containing a summary of several different studies. Only two tester strains used.

References

Yam, J., K. A. Booman, W. Broddle, L. Geiger, J. E. Heinze, Y. J. Lin, K. McCarthy, S. Reiss, V. Sawin, R. I. Sedlak, R. S. Slesinski and G. A. Wright. 1984. Surfactants: A Survey of Short-Term Genotoxicity Testing. Fd Chem. Toxic. (22)9:761-769.

Other

Last changed: December 13, 2001
Order number for sorting: 6a
Remarks:

5.5 Genetic Toxicity *In vitro* - Mutagenicity

Test Substance

Identity:	Cetyltrimethylammonium chloride (CAS RN 112-02-7; Ammonium, hexadecyltrimethyl-, chloride)
Purity:	99.30%
Remarks:	

Method

Method/Guideline followed:	Ames, B., J. McCann and E. Yamasaki. 1975. Mut. Res. 31:347 with some modification (Yahagi, T. 1975. Protein, Nucleic Acid and Enzyme. 20:1178).
Type:	Reverse mutation assay
System of testing:	Bacterial
GLP:	Not stated
Year:	1980
Species/Strain:	*Salmonella typhimurium* TA98 and TA100
Metabolic activation:	With and without S9 activation
Concentrations tested:	0.05, 0.1, 0.5, 1.0, 5.0 and 10.0 µg/plate
Statistical methods:	None
Remarks:	Preincubation assay was used. Vehicle used was distilled water or dimethylsulphoxide.

Results

Result:	Negative
Cytotoxic concentration:	5.0 µg/plate without metabolic activation
Genotoxic effects:	None
Statistical results:	None
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles. Only two tester strains used.

References

Inoue, K., T. Sunakawa and S. Takayama. 1980. Studies of *In Vitro* Cell Transformation and Mutagenicity by Surfactants and Other Compounds. Fd. Cosmet. Toxicol. 18:289 - 296.

Other

Last changed: December 13, 2001
Order number for sorting: 7a – mut.
Remarks:

5.5 GENETIC TOXICITY *IN VITRO* - TRANSFORMATION

Test Substance

Identity:	Cetyltrimethylammonium chloride (CAS RN 112-02-7; Ammonium, hexadecyltrimethyl-, chloride)
Purity:	99.30%
Remarks:	

Method

Method/Guideline followed:	Pienta, R. J., J. A. Poiley and W. B. Lebherz. 1977. Morphological transformation of early passage golden Syrian hamster embryo cells derived from cryopreserved primary cultures as a reliable in vitro bioassay for identifying diverse carcinogens. Int. J. Cancer. 19:642.
Type:	*In vitro* transformation
System of testing:	Nonbacterial
GLP:	Not stated
Year:	1980
Species/Strain:	Cryopreserved primary hamster embryo cells
Metabolic activation:	Not applicable
Concentrations tested:	0.1, 1.0 and 5.0 µg/ml
Statistical methods:	None
Remarks:	On Day 0, an ampule of cryopreserved primary cells prepared as feeder-layer cells was rapidly thawed and plated in a 75-cm^2 flask containing 20 ml of culture medium. On day 3, an ampule of cryopreserved primary cells prepared as target cells was also rapidly thawed and plated in a 75-cm^2 flask. On day 4, the feeder cells which were shifting from a stage of logarithmic growth to a stationary phase were irradiated with 5000 R from a linear accelerator, trypsinized, and then plated at 6×10^4 cells/50-mm dish in 2 ml of complete medium. On day 5, the target cells which were approximately 80 - 90% confluent were trypsinized and a suspension of 500 target cells in 2 ml of complete medium was then added to each of the dishes plated the day before with irradiated feeder-layer cells. On day 6, an appropriate dose of the test chemical in a volume of 4 ml was added. Nine dishes were used for each dose level. On day 14, the cultures were fixed with absolute methanol for 10 minutes and stained with Giemsa solution for 45 minutes or more. The stained dishes were examined with a stereoscopic dissection microscope to count normal

and transformed colonies. Randomly oriented three-dimensional growth with extensive crossing-over of the cells at the periphery of the colony was considered to be the endpoint of morphological transformation.

Results

Result:	Negative. Cetyltrimethylammonium chloride did not produce transformation at any of the doses tested.
Cytotoxic concentration:	5.0 µg/ml
Genotoxic effects:	None
Statistical results:	None
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References

Inoue, K., T. Sunakawa and S. Takayama. 1980. Studies of *In Vitro* Cell Transformation and Mutagenicity by Surfactants and Other Compounds. Fd. Cosmet. Toxicol. 18:289 - 296.

Other

Last changed:	December 13, 2001
Order number for sorting:	7a – trans.
Remarks:	

5.5 GENETIC TOXICITY *IN VITRO*

Test Substance

Identity:	ARQUAD T-50 (CAS RN 8030-78-2; Quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	Reverse mutation assay
System of testing:	Bacterial
GLP:	Yes
Year:	1983
Species/Strain:	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537 and TA1538
Metabolic activation:	With and without S9 activation
Concentrations tested:	Not stated
Statistical methods:	None
Remarks:	Plate incorporation assay

Results

Result:	Negative
Cytotoxic concentration:	Not stated
Genotoxic effects:	None
Statistical results:	None
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions; peer review article containing a summary of several different studies.

References	Yam, J., K. A. Booman, W. Broddle, L. Geiger, J. E. Heinze, Y. J. Lin, K. McCarthy, S. Reiss, V. Sawin, R. I. Sedlak, R. S. Slesinski and G. A. Wright. 1984. Surfactants: A Survey of Short-Term Genotoxicity Testing. Fd Chem. Toxic. (22)9:761-769.

Other

Last changed:	December 13, 2001
Order number for sorting:	16a
Remarks:	

5.5 GENETIC TOXICITY *IN VITRO*

Test Substance

Identity:	ARQUAD T-50 (CAS RN 8030-78-2; Quaternary ammonium compounds, trimethyltallow alkyl, chlorides)
Purity:	50%
Remarks:	

Method

Method/Guideline followed:	Ames, B. N. et al. 1975. Mut. Res. 31:347.
Type:	Reverse mutation assay
System of testing:	Bacterial
GLP:	Yes
Year:	1982
Species/Strain:	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537 and TA1538
Metabolic activation:	With and without S9 activation
Concentrations tested:	Not stated.
Statistical methods:	None
Remarks:	The test was run in triplicate and a three-fold increase in back mutations was considered as the criterion for a positive test for mutagenicity. Plate incorporation assay was used. Vehicle used was dimethylsulphoxide.

Results

Result:	Positive
Cytotoxic concentration:	500 µg/plate
Genotoxic effects:	Positive at 50 µg/plate with TA1538 with and without S9 activation. Negative at all concentrations with TA98, TA100, TA1535 and TA1537
Statistical results:	None
Remarks:	The positive result observed with TA1538 at 50 µg/plate may be due to the surfactant itself or impurities arising during its manufacture.

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References

Kaplan, D. L. and A. M. Kaplan. 1982. Mutagenicity of 2,4,6-Trinitrotoluene-Surfactant Complexes. Bull. Environ. Contam. Toxicol. 28:33-38.

Other

Last changed:	December 13, 2001
Order number for sorting:	17
Remarks:	

5.5 Genetic Toxicity *In vitro*

Test Substance

Identity:	Stearyltrimethylammonium chloride (CAS RN 112-03-8; Trimethyloctadecylammonium chloride).
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Type:	Reverse mutation assay
System of testing:	Bacterial
GLP:	Yes
Year:	1983
Species/Strain:	*Salmonella typhimurium* TA98 and TA100
Metabolic activation:	With and without S9 activation
Concentrations tested:	Not stated
Statistical methods:	None
Remarks:	Plate incorporation assay

Results

Result:	Negative
Cytotoxic concentration:	Not stated
Genotoxic effects:	None
Statistical results:	None
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions; peer review article containing a summary of several different studies. Only two tester strains used.

References

Yam, J., K. A. Booman, W. Broddle, L. Geiger, J. E. Heinze, Y. J. Lin, K. McCarthy, S. Reiss, V. Sawin, R. I. Sedlak, R. S. Slesinski and G. A. Wright. 1984. Surfactants: A Survey of Short-Term Genotoxicity Testing. Fd. Chem. Toxic. (22)9:761-769.

Other

Last changed: December 13, 2001
Order number for sorting: 9a
Remarks:

5.5 GENETIC TOXICITY *IN VITRO*

Test Substance

Identity:	ARQUAD 2C-75 (CAS RN 61789-77-3; Quaternary ammonium compounds, dicoco alkyldimethyl, chlorides)
Purity:	76.4%
Remarks:	

Method

Method/Guideline followed:	OECD Guideline No. 471 and Annex V of the EEC Directive 67/548/EEC, Part B
Type:	Reverse mutation assay
System of testing:	Bacterial
GLP:	Yes
Year:	1990
Species/Strain:	*Salmonella typhimurium* TA98, TA100, TA1535 and TA1537
Metabolic activation:	With and without S9 activation; S-9 mix obtained from the liver of Aroclor 1254-induced rats
Concentrations tested:	33.3, 10.0, 3.3, 1.0, and 0.33 µg/plate in the presence of S-9 mix and 10.0, 3.3, 1.0, 0.33 and 0.1 µg/plate in the absence of S-9 mix
Statistical methods:	None
Remarks:	Vehicle used was dimethylsulphoxide. Positive controls with S9 activation were sodium azide (TA1535), 9-aminoacridine (TA1537), daunomycine (TA98) and methylmethanesulfonate (TA100). The positive control substances used without S9 activation were 2-aminoanthracene for all tester strains. The S-9 homogenate and S-9 mix were prepared in-house. Direct plate incorporation method was utilized. The doses tested in the mutagenicity assay were selected based on the results of a dose range-finding study using tester stain TA100 and nine dose levels of the test substance ranging from 5000 to 1.0 µg/plate, both in the presence and absence of S-9 mix. Based on the results of the range-finding study the test substance was tested up to a concentration of 33.3 µg/plate in the presence of S-9 mix and up to 10.0 µg/plate in the absence of S-9 mix. The assay was conducted with five doses of test substance in both the presence and absence of S-9 mix along with concurrent vehicle and positive controls using three plates per dose. The results of the mutagenicity assay were confirmed in an independent experiment.

Results

Result:	Negative
Cytotoxic concentration:	100 µg/plate and above in the presence of S-9 mix and 33.3 µg/plate and above in the absence of S-9 mix
Genotoxic effects:	None
Statistical results:	None
Remarks:	The results of the preliminary screen: In the absence of S-9 mix, the survival of strain TA100 was not or was only slightly reduced up to test substance concentration of 10.0 µg/plate and eliminated at and above 33.3 µg/plate. In the presence of S-9 mix, the survival of strain TA100 was slightly reduced at a test substance concentration of 33.3 µg/plate and eliminated at and above 100 µg/plate. All bacterial strains showed negative responses over the entire dose range of the test substance with and without S-9 activation. The negative and positive controls validated the test systems and the metabolic activation system.

Conclusions

Remarks:	Based on the results of this study, it is concluded that the test substance can be considered as not mutagenic in the Ames *Salmonella*/microsome assay. (Author of the study report). The endpoint has been adequately characterized (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; guideline study.

References

Scheres, H. M. E. 1990. Evaluation of the Mutagenic Activity of ARQUAD 2C-75 in the Ames Salmonella/Microsome Test. RCC NOTOX Project 031455. RCC NOTOX B.V. ‘s-Hertogenbosch, The Netherlands.

Other

Last changed:	December 13, 2001
Order number for sorting:	17p
Remarks:	

5.5 GENETIC TOXICITY *IN VITRO*

Test Substance

Identity:	Tricetylmethyl ammonium chloride (CAS RN 52467-63-7)
Purity:	39.7%
Remarks:	

Method

Method/guideline followed:	A modification of that described by Ames *et al.*, 1975
Type:	Reverse mutation assay
System of testing:	Bacterial
GLP:	Yes
Year:	1990
Species/Strain:	*Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100; *Escherichia coli* strain WP2*uvr*A
Metabolic activation:	With and without S-9 activation; S-9 mix obtained from the liver of Aroclor 1254-induced male Sprague Dawley rats; S-9 mix was prepared at the laboratory; 0.5 ml/plate was used.
Concentrations tested:	333, 667, 1000, 3333 and 5500 μg/plate
Statistical methods:	Mean and standard deviation
Remarks:	Two independent experiments (initial and confirmatory assays) were conducted and three replicates per dose were tested in each experiment. Plates were dosed once. In both experiments, the test substance was tested in the vehicle, ethanol. The experiments were conducted in the absence and in the presence of metabolic activation. Ethanol was tested as the negative control for each tester strain in the absence and in the presence of metabolic activation. Positive control plates were included for each strain. The following concentrations and substances were used as positive controls without metabolic activation: 1 μg/plate Na-azide (TA100 and TA1535), 2 μg/plate ICR-191 (TA1537), 1 μg/plate 2-nitrofluorene (TA98 and TA1538) and 1000 μg/plate methyl methanesulfonate (WP2*uvr*A). The following concentrations and substances were used as positive controls with metabolic activation: 0.5 μg/plate 2-aminoanthracene (TA98, TA100, TA1535, TA1537 and TA1538) and 10000 μg/plate 2-aminoanthracene (WP2*uvr*A). For a test substance to be evaluated positive, it must cause a dose-related increase in the mean revertants per plate of at least one tester strain with a minimum of two increasing concentrations of test substance as follows: For strains TA1535, TA1537 and TA1538, data sets were judged positive if the increase in mean revertants at the

peak of the dose response was equal to or greater than three times the mean vehicle control value. For strains TA98, TA100 and WP2*uvr*A, data sets were judged positive if the increase in mean revertants at the peak of the dose response was equal to or greater than two times the mean vehicle control values.

Dose range-finding study
A dose-range-finding study was conducted with tester strains TA100 and WP2*uvr*A. Ten dose levels of the test substance ranging from 6.7 to 5000 µg/plate were evaluated. No cytotoxicity or genotoxic effects were evident at any dose level tested up to 5000 µg/plate.

Results

Result: The test substance was not mutagenic in the bacterial test system either in the absence or in the presence of metabolic activation under the conditions of this test.

Cytotoxic concentration: None

Genotoxic effects: Negative (with and without metabolic activation)

Statistical results: None

Remarks: Moderate precipitation was observed in the 3333 and 5000 µg/plate in all experiments with all tester strains, which required the manual counting of revertants. Slight precipitation was noted at dose levels as low as 333 µg/plate.

Conclusions

Remarks: When tested at dose levels up to 5500 µg/plate in ethanol, tricetylmethyl ammonium chloride was not mutagenic in this bacterial test system. (Author of report)
The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1B

Remarks: Reliable without restriction; comparable to guideline study.

References

San, R. H. C. 1990. *Salmonella*/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (Ames Test) and *Escherichia coli* WP2*uvr*A Reverse Mutation Assay. Study number T9115.501038. Microbiological Associates, Inc., Rockville, MD, U. S.

Other

Last changed:	May 29, 2001
Order number for sorting:	29
Remarks:	

5.6 GENETIC TOXICITY *IN VIVO*

Test Substance

Identity:	P1232 (CAS RN 112-00-5; Ammonium, dodecyltrimethyl-, chloride).
Purity:	24.7% aqueous solution
Remarks:	

Method

Method/Guideline followed:	Not specified
Type:	Bone marrow cytogenetic assay
GLP:	Yes
Year:	1982
Species:	Rat
Strain:	Sprague-Dawley
Sex:	Male and female
Route of administration:	Oral gavage
Doses/concentration levels:	16, 53.3, 160 mg/kg
Exposure period:	5 days
Statistical methods:	None
Remarks:	The test substance was administered via oral gavage to five male and five female rats once daily for 5 consecutive days at doses of 16, 53.3 or 160 mg/kg. The test substance was dosed at a constant volume of 0.58 ml of solution in distilled water/150 grams of body weight. Five animals/sex were administered the negative control, distilled water and the positive control, methylmethane sulfonate (80 mg/kg/day). An intraperitoneal injection of colchicine (1 mg/kg) was given to all animals to inhibit mitosis approximately 20 hours after the last treatment. The animals were sacrificed 2-4 hours later. Bone marrow cells were examined microscopically for structural chromosome aberrations. Fifty metaphase spreads for each animal were scored when possible. The mitotic index (MI) for each animal was determined. Each metaphase figure was scored for the number of chromosomes, and aberrations were categorized.

Results

Effect on mitotic index:	None
Genotoxic effects:	None
NOEL:	160 mg/kg/day
Statistical results:	None
Remarks:	Animals receiving the test compound and the positive control substance showed no signs of toxicity.

Conclusions

Remarks: It can be concluded that the test material did not induce a significant number of chromosomal aberrations, indicating that it has no mutagenic potential. (Author of report)
The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 1B
Remarks: Reliable without restriction; comparable to guideline study.

References

Esber, H. J. 1982. In vivo cytogenetics study in rats. EG&G/Mason Research Institute, Worcester, MA, USA. Unpublished report MRI-174-PG-82-53.

Other

Last changed: September 12, 2001
Order number for sorting: 2c4
Remarks:

5.6 GENETIC TOXICITY *IN VIVO*

Test Substance

Identity:	Ditallow dimethyl ammonium chloride (CAS RN 68783-78-8; Quaternary ammonium compounds, dimethylditallow alkyl, chlorides;)
Purity:	74.1% in water/isopropanol
Remarks:	

Method

Method/Guideline followed:	None
Type:	Cytogenetic assay (*in vivo* micronucleus assay)
GLP:	No
Year:	1976
Species:	Mouse
Strain:	$C_3D_2F_1$/J
Sex:	Male
Route of administration:	Oral (gavage)
Doses/concentration levels:	0, 50 , 500, 1000 mg/kg
Exposure period:	Two doses 24 hours apart; sacrifice 6 and 24 hours after the second dose.
Statistical methods:	Analysis of variance
Remarks:	Eight mice/group were used. Animals were dosed twice (24 hours apart) with 0, 50, 500 or 1000 mg/kg via gavage. Saline was used as the control vehicle. Dosing volume was 0.2 ml/dose. Six hours after the second dosing, one group at each dose was sacrificed. The remaining groups were sacrificed 24 hours after the second dose. Immediately after sacrifice, bone marrow cells were extracted from both femurs and processed. One thousand polychromatic erythrocytes were scored from each mouse and micronuclei were recorded.

Results

PCE/NCE ratio:

Dose Group	PCE/NCE
Negative control	
6 hour	0.22
24-hour	0.17
50 mg/kg	
6 hour	0.09
24-hour	0.22
500 mg/kg	
6 hour	0.11
24-hour	0.23
1000 mg/kg	
6 hour	0.14
24-hour	0.21

Genotoxic effects: Negative
NOAEL (NOEL): 1000 mg/kg
Statistical results: There were no statistically significant differences in the mean micronuclei of the test groups compared to the negative control group.
Remarks:

Conclusions

Remarks: The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch): 2A
Remarks: Reliable with restriction; acceptable, well-documented study report that meets basic scientific principles.

References

Wong, T.K. and Thompson, E.D. 1977. In vivo mouse micronucleus assay of ditallow dimethyl ammonium chloride (DTDMAC) for mutagenic potential. P&RS Division. Unpublished report BSBTS #114.

Other

Last changed: September 11, 2001
Order number for sorting: 25a1
Remarks:

5.6 Genetic Toxicity *In vivo*

Test Substance

Identity:	Tricetylmethyl ammonium chloride (CAS RN 52467-63-7)
Purity:	39.7%
Remarks:	

Method

Method/Guideline followed:	OECD Guidelines, 1984, *In vivo* mammalian bone marrow cytogenetic test – chromosomal analysis; EPA Guidelines, 1985, Federal Register 50, pp. 39445 – 39446; and EPA Proposed Guidelines, 1986, Federal Register 51, pp. 1540 – 1541
Type:	Bone marrow cytogenetic assay
GLP:	Yes
Year:	1990
Species:	Rat
Strain:	Sprague-Dawley
Sex:	Male and female
Route of administration:	Oral gavage
Doses/concentration levels:	5 g/kg
Exposure period:	Single administration
Statistical methods:	Fisher's exact test; Wilcoxon's rank sum test
Remarks:	A single dose of the test substance was administered via oral gavage to ten male and ten female rats at a dose level of 5 g/kg. The test substance was dosed as a 40% suspension in mineral oil at a constant volume of 12.5 ml/kg. This maximum tolerated dose (MTD) was determined in a range-finding study. Since the test substance was found to be nontoxic in this study, the high dose level of 5 g/kg was used. Ten males and ten females were administered the vehicle control alone. Ten males and ten females were administered the negative control, distilled water. Five males and five females were administered the positive control, cyclophosphamide (20 mg/kg). Ten to 12 week old male and female rats weighed 270 – 305g and 190 – 250 g, respectively, before dosing. Bone marrow cells, arrested in metaphase and collected 8 and 12 hours after treatment, were examined microscopically for structural chromosome aberrations. (Note: The selection of two harvest times did not follow the current OECD Guidelines, but it did agree with the proposed EEC Guidelines, EEC Directive 79/831. Annex V. Test B.10. Update of June 1989.) If possible, a total of 50 metaphase spreads for each animal were scored. The mitotic index (MI) for each animal was determined. Each

metaphase figure was scored for the number of chromosomes, and aberrations were categorized.

Results

Effect on mitotic index:

Group	Harvest time (hours)	Sex	Mitotic Index (mean ± SD)
Water 12.5 ml/kg	8 8	Male Female	2.4 ± 0.7 2.0 ± 1.3
Mineral Oil 12.5 ml/kg	8 8	Male Female	2.0 ± 0.3 1.7 ± 0.6
Tricetylmethyl ammonium chloride 5 g/kg	8 8	Male Female	2.3 ± 0.2 2.2 ± 1.2
Water 12.5 ml/kg	12 12	Male Female	1.3 ± 0.6 1.5 ± 0.5
Mineral Oil 12.5 ml/kg	12 12	Male Female	1.6 ± 0.6 1.8 ± 1.3
Tricetylmethyl ammonium chloride 5 g/kg	12 12	Male Female	1.8 ± 0.5 1.7 ± 0.9

Genotoxic effects: None

NOEL: 5 g/kg

Statistical results: Described below

Remarks: The test substance had no effect on body weight gain within 12 hours of administration. Diarrhea was observed in many of the animals receiving the test substance in mineral oil as well as mineral oil alone. There was no indication of bone marrow toxicity, as evidenced by the absence of inhibition of mitosis. No statistically significant increases in percentage of aberrant cells were observed in the test substance-treated groups, regardless of sex or bone marrow harvest time.

Conclusions

Remarks: Under the conditions of this test, the test substance did not induce chromosomal aberrations in bone marrow cells of male or female rats. (Author of report)
The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	1A
Remarks:	Reliable without restriction; guideline study.

References

Putman, D. L. 1990. Cytogenicity Study – Rat Bone Marrow *In-vivo*. Study number T9115.105. Microbiological Associates, Inc., Bethesda, MD, U. S.

Other

Last changed:	May 11, 2001
Order number for sorting:	28
Remarks:	

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Test Substance

Identity:	C12-14 trimethyl ammonium chloride (CAS RN 112-00-5; Ammonium, dodecyltrimethyl-, chloride)
Purity:	35% in Dobanol 45E7
Remarks:	CAS RN 112-00-5 is considered appropriate for this chemical although it is a mixture of C12 – C14 isomers

Method

Method/Guideline followed:	Not stated
GLP:	No
Year:	1979
Species:	Rabbit
Strain:	New Zealand White
Route of administration:	Oral (gavage)
Doses/concentration levels:	2, 8, 24 mg/kg/day – definitive study 25, 50, 100, 200, 400 mg/kg/day – range-finding study
Sex:	Female
Exposure period:	Days 6 - 18 of gestation
Frequency of treatment:	Daily
Control group and treatment:	Yes, water
Duration of test:	Days 0 - 29 of gestation
Statistical methods:	None
Remarks:	Definitive Study: Thirteen or 14 mated female rabbits per group were exposed to the test substance orally at doses of 0, 2, 8 and 24 mg/kg/day for days 6 through 18 of gestation. The control group was treated with deionized water only. Animals were observed daily for signs of toxicity. Body weights were taken every three days during pregnancy. Food consumption was measured daily. All surviving dams were sacrificed at study termination on gestation day 29 using sodium pentobarbital. An examination of the uterus, including the number corpora lutea, implantations, and resorptions was conducted. Uteri from females that appeared non-gravid were placed in 10% ammonium sulfide solution for confirmation of pregnancy. At sacrifice fetuses were weighed, and examined externally for defects. Sex determination also was conducted on each fetus. Two thirds of the fetuses were examined for skeletal and 1/3 were examined for visceral abnormalities.

	Range-Finding Study: Three mated female rabbits per group were exposed to the test substance orally at doses of 0, 25, 50, 100, 200 or 400 mg/kg/day for days 6 through 18 of pregnancy. Body weights were determined on days 0, 6, 11, 17 and 29. Food consumption was measured daily. Animals found dead were necropsied; survivors were sacrificed on day 29 of gestation and fetuses were weighed and examined microscopically. Uterine disposition of young was recorded, and corpora lutea and resorptions sites were counted.

Results

Maternal toxicity NOEL:	24 mg/kg/day
Developmental toxicity NOEL:	24 mg/kg/day
Actual dose received:	2, 8 and 24 mg/kg/day
Maternal data:	Definitive Study: No effects related to treatment were observed at the doses used in this study. Range-Finding Study: Morality occurred in the dams as follows: 1/3, 1/3, 2/3, 3/3, and 3/3 for the 25, 50, 100, 200, and 400 mg/kg/day groups, respectively. A decrease in body weight was observed at 50 and 100 mg/kg/day. Apparent resorptions occurred in the two surviving females at 50 mg/kg/day but the intercurrent mortality was considered to prohibit definitive judgment on a direct effect of the test substance on maintenance of pregnancy.
Fetal data:	Definitive Study: No effects on any parameters were attributed to treatment with the test substance. Range-Finding Study: An indirect embryotoxic effect based on fetal body weight was considered to have been exhibited at 50 mg/kg/day.
Statistical results:	None
Remarks:	This study does not conform to guidelines for developmental toxicity studies and is of limited scope. However, it provides supporting information for the FND Cationics Chemical Category.

Conclusions

Remarks:	Within the limitations of the experimental conditions used, the test substance was not directly fetotoxic or teratogenic. The data support the overall category. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report that meets basic scientific principles.

References

Preliminary teratology study in rabbits with E 9060, ECM BTS 280. 1979. IFREB (Institut Francais de recherches et Essais Biologiques), Lyon, France. Unpublished report (No. 908251).

Other

Last changed:	September 13, 2001
Order number for sorting:	2d
Remarks:	

5.9 Developmental Toxicity/Teratogenicity

Test Substance

Identity:	G0087.02 (CAS RN 112-02-7; Ammonium, hexadecyltrimethyl-, chloride)
Purity:	Citrimonium chloride (25%) - 100%
Remarks:	Assume based on similar chemicals that this is a 25% aqueous solution of the test chemical.

Method

Method/Guideline followed:	Not stated
GLP:	Yes
Year:	1985
Species:	Rabbit
Strain:	New Zealand White
Route of administration:	Dermal
Doses/concentration levels:	0.5, 1.0 and 2.0% at 2.0 ml/kg (10, 20 and 40 mg/kg/day)
Sex:	Female
Exposure period:	Days 7 - 18 of gestation
Frequency of treatment:	Daily
Control group and treatment:	Yes, deionized water
Duration of test:	Days 0 - 29 of gestation
Statistical methods:	Body weight changes and food consumption and number of early and late resorptions, dead fetuses, total implantations, corpora lutea, skeletal abnormalities, and mean fetal body weight were compared by analysis of variance (Bartlette's). If variance was not significant, then treatment-control comparisons were made using the least significant difference (LSD) criterion. If variance was significant, then comparisons were made using the t-test for unequal variances and the Wilcoxon, Mann-Whitney rank sum test. Additionally, a regression and lack of fit were performed on each of these parameters. The number of pregnancies per group, the percentage of skeletal abnormalities and soft tissue malformations were compared in each treated group to the control group by Fisher's exact test. A 5% two-sided risk was used.
Remarks:	Twenty mated female rabbits per group were exposed for days 7 through 18 of gestation to 2.0 ml/kg of the test substance topically at concentrations of 0, 0.5, 1.0, or 2.0%. These doses corresponded to daily exposures of 0, 10, 20 and 40 mg/kg/day, respectively. The control group was treated with deionized water only. Prior to the initial treatment, the dorsal area of each animal was shaved and any skin lesions were documented. At the time of treatment, the animals were fitted with a collar to prevent

oral ingestion of the test substance. After the 2-hour exposure period, the collars were removed and the application site was rinsed with water and dried. Animals were observed twice daily for signs of toxicity, including skin irritation from days 7 through 29. Body weights were taken on gestation days 0, 3, 6, 9, 12, 15, 18, 21, 24, 27 and 29. Individual food consumption was measured daily. A gross necropsy was conducted on animals that died in an attempt to determine the cause of death. Fetuses less than 28 days old were fixed in buffered neutral formalin and those 28 days or older were cleared and stained. All surviving dams were sacrificed at study termination on gestation day 29 using sodium pentobarbital. An examination of the uterus (including the number and location of live and dead fetuses, early and late resorptions, and implantation sites), and ovaries (including the number of corpora lutea), was conducted. Following removal of the fetuses the abdominal and thoracic cavities and organs of the dams were examined. Uteri from females that appeared non-gravid were placed in 10% ammonium sulfide solution for confirmation of pregnancy. At sacrifice fetuses were identified, weighed, and examined externally for defects. Gross dissection and examination of viscera, and internal sex determination also were conducted on each fetus. Finally, an examination of the skeleton for anomalies and ossification variations was conducted after clearing and alizarin red staining of the fetuses.

Results

Maternal toxicity NOEL: 2% (40 mg/kg/day) except for skin irritation

Developmental toxicity NOEL: 2% (40mg/kg/day)

Actual dose received: approximately 10, 20 and 40 mg/kg/day

Maternal data: Two control, one intermediate and one high dose doe died during the study. The cause of death could not be determined. Two of the does that died aborted prior to death (one control and one intermediate dose group animal). Two additional abortions occurred, one each in the intermediate and high dose groups. None of these deaths or abortions were considered related to test substance toxicity. Skin irritation was observed at all doses with the severity and duration of erythema, edema, desquamation, atonia and coriaceousness increased in a dose-dependent manner. No treatment-related maternal body weight or food intake effects were noted. A slight increase in congested lungs was observed for the high dose group at necropsy.

Fetal data:	The incidence of fetal malformation and genetic and developmental variation in the treated groups was comparable to that of the control group. No other treatment-related effects were noted.
Statistical results:	Described above
Remarks:	This study used an exposure of 2 hours per day.

Conclusions

Remarks:	Within the limitations of the experimental conditions used, the test substance was not fetotoxic or teratogenic. The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report that meets basic scientific principles.

References

Aldridge, D. 1985. International Research and Development Corporation, Mattawan, MI, USA. Unpublished report no. 191-856.

Other

Last changed:	September 13, 2001
Order number for sorting:	7f
Remarks:	

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Test Substance

Identity:	Trimethylstearylammonium chloride (CAS RN 112-03-8)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
GLP:	Not stated
Year:	1983
Species:	Rat
Strain:	CFY Sprague-Dawley
Route of administration:	Dermal
Doses/concentration levels:	0.9, 1.5 and 2.5% (dose volume 0.5 ml) (approximately 4.5, 7.5 and 12.5 mg/kg/day)
Sex:	Female
Exposure period:	Days 6 - 15 of gestation
Frequency of treatment:	Daily
Control group and treatment:	Yes (concurrent, dosed with distilled water at a dose volume of 0.5 ml/rat)
Duration of test:	Days 0 – 20 of gestation
Statistical methods:	Not stated
Remarks:	Concentrations (w/v) of 0.9, 1.5 and 2.5% of the test substance in distilled water were utilized for this study. All animals were dosed with 0.5 ml of the proper test substance concentration from day 6 to 15 of gestation. The test substance was applied with a syringe and gently massaged into the shaved area (4 x 4 cm) of skin in the scapula region for not more than one minute. The test substance was left on the skin and was neither removed by washing nor occluded. Twenty mated female rats per group resulted in 10 to 20 pregnant dams per group that provided between 192 and 259 live fetuses per group for examination. All animals were observed for signs of systemic and local reactions. Body weights, food and water consumption were recorded at regular intervals throughout the study. On day 20 of gestation, dams were killed, litter values determined and fetuses subsequently examined for visceral and skeletal abnormalities.

Results

Maternal toxicity NOEL:	> 2.5% in 0.5 ml (approximately > 12.5 mg/kg/day)
Developmental toxicity NOEL:	> 2.5% in 0.5 ml (approximately > 12.5 mg/kg/day)
Actual dose received:	Not stated
Maternal data:	There were no systemic signs of toxicity, no deaths or treatment-related macroscopic pathology changes in internal organs were noted. A dosage-related local reaction was recorded in terms of incidence of animals affected and degree of erythema and edema. The initial reaction was evident within a day of the first administration, reaching a peak around the mid-point of the dosing period; thereafter, stabilizing or declining. There was no marked or consistent treatment-related difference in weight gain, although marginally lower weight gains during the dosing period were observed in all treated groups. There was no marked effect on food or water consumption.
Fetal data:	Litter values assessed by litter size, post-implantation loss, litter and mean fetal weights and the embryonic and fetal development were not affected by treatment with the test substance. There were no significant differences from concurrent control values in respect of the incidence of malformed or anomalous young or of litters containing affected young. The types of malformation or anomaly observed were compatible with the types of abnormality recorded among concurrent or historical control values.
Statistical results:	Not stated.
Remarks:	

Conclusions

Remarks:	Within the limitations of the experimental conditions used, it was concluded that trimethylstearylammonium chloride exerted no selective embryopathic activity when applied topically to pregnant rats during the organogenic period (days 6 to 15 of gestation). (Author of the study report) The endpoint has been adequately characterized. (American Chemical Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References

Palmer, A. K., A. M. Bottomley, J. A. Edwards and R. Clark. 1983. Absence of Embryotoxic Effects in Rats with Three Quarternary Ammonium Compounds (Cationic Surfactants). Toxicology 26:313 - 315.

Other

Last changed:	December 13, 2001
Order number for sorting:	9b
Remarks:	

5.9 Developmental Toxicity/Teratogenicity

Test Substance

Identity:	XSA-201 (CAS RN 68783-78-8; Quaternary ammonium compounds, dimethylditallow alkyl, chlorides)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
GLP:	No
Year:	1975
Species:	Rat
Strain:	CD Sprague-Dawley
Route of administration:	Oral (gavage and diet)
Doses/concentration levels:	100 and 500 mg/kg/day (oral gavage) 0.65% active ingredient (oral diet); 508 mg/kg/day
Sex:	Female
Exposure period:	Days 6 - 13 or 6 - 18 of gestation
Frequency of treatment:	Daily
Control group and treatment:	Yes (concurrent, 15% isopropanol for gavage control; control diet for dietary exposure)
Duration of test:	Days 0 – 21 of gestation
Statistical methods:	Comparisons between control and test groups were made where applicable by the Chi-square method. Maternal body weight gains, total litter weights and mean fetal weights were compared to control by the F-test and Student's t-test. When variances differed significantly, Student's t-test was appropriately modified, and Cochran's approximation was utilized.
Remarks:	Female rats were administered the test substance either by oral gavage at dose levels of 100 and 500 mg active ingredient/kg body weight/day (the vehicle was 15% isopropanol) or in the diet at a dose level of 0.65% active ingredient beginning on day 6 of gestation. Two control groups were run concurrently; one receive the gavage vehicle and the other received control feed only. Ten rats per group were sacrificed after the day 13 treatment and 15 rats per group were treated through day 18 and sacrificed on day 21 of gestation. Body weights were taken on days 0, 6, 9, 12, 15, 18 and 21 of gestation. Food consumption was evaluated for days 12 and 18 of gestation. Clinical observations were made daily for signs of pharmacologic or toxicologic effect and mortality. Gross necropsies were conducted on all surviving rats, moribund rats and rats that died spontaneously. At necropsy, for rats

sacrificed on day 13 of gestation, the uterus (number and location for each horn of resorptions, embryos and implantation sites) and ovaries (number of corpora lutea of pregnancy per ovary) were observed. At necropsy, for rats sacrificed on day 21 of gestation, the uterus (number and location for each horn of live fetuses, dead fetuses, early and late resorptions and implantation sites) and ovaries (number of corpora lutea of pregnancy per ovary) were observed. The necropsy for all maternal rats also included observations for obvious abnormalities and the following tissues were examined: heart, lung, stomach, liver, pancreas, spleen, mesenteric lymph nodes, jejunum, kidney, adrenal, bladder and ovary.

Results

Maternal toxicity NOEL:	> 500 mg/kg/day by gavage; none established for diet
Developmental toxicity NOEL:	> 500 mg/kg/day by gavage; > 508 mg/kg/day via diet
Actual dose received:	100 or 500 mg/kg/day by gavage; 508 mg/kg/day via diet
Maternal data:	Depressed body weight gains during gestation were noted in the group that received the test substance in the diet; food consumption values also were less in this group than in the group that received control feed. No adverse effects attributable to compound administration were noted in comparisons of pregnancy and mortality rates. Early deliveries and abortions, necropsy findings, and reproduction data were considered not to be affected by treatment with the test substance. An increase in resorptions was observed for the 100 mg/kg/day gavage group compared to the isopropanol control group (7.1% vs 2.1%). This difference was not considered a treatment-related effect due to the lack of dose response and a low value for the control group compared to historical data from the laboratory.
Fetal data:	No differences considered to be related to the administration of the test substance were noted in fetal size and sex, variations in degree of ossification or malformations.
Statistical results:	Described above
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A
Remarks:	Reliable with restrictions; acceptable, well-documented publication/study report that meets basic scientific principles.

References

Killeen, J. C., Jr. and W. R. Rapp. 1975. A Rat Teratology Study of XSA-201-202. Project number 73R-927. Bio/dynamics Inc.

Other

Last changed:	December 13, 2001
Order number for sorting:	25b
Remarks:	

5.9 Developmental Toxicity/Teratogenicity

Test Substance

Identity:	XSA-202 (CAS RN 61789-81-9; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, Me sulfates)
Purity:	
Remarks:	

Method

Method/Guideline followed:	Not stated
GLP:	No
Year:	1975
Species:	Rat
Strain:	CD Sprague-Dawley
Route of administration:	Oral (gavage and diet)
Doses/concentration levels:	100 and 500 mg/kg/day (oral gavage) 0.55% active ingredient (oral diet); 475 mg/kg/day
Sex:	Female
Exposure period:	Days 6 - 13 or 6 - 18 of gestation
Frequency of treatment:	Daily
Control group and treatment:	Yes (concurrent, 15% isopropanol for gavage control; control diet for dietary exposure)
Duration of test:	Days 0 - 21 of gestation
Statistical methods:	Comparisons between control and test groups were made where applicable by the Chi-square method. Maternal body weight gains, total litter weights and mean fetal weights were compared to control by the F-test and Student's t-test. When variances differed significantly, Student's t-test was appropriately modified, and Cochran's approximation was utilized.
Remarks:	Female rats were administered the test substance either by oral gavage at dose levels of 100 and 500 mg active ingredient/kg body weight/day (the vehicle was 15% isopropanol) or in the diet at a dose level of 0.55% active ingredient beginning on day 6 of gestation. Two control groups were run concurrently; one received the gavage vehicle and the other received control feed only. Ten rats per group were sacrificed after the day 13 treatment and 15 rats per group were treated through day 18 and sacrificed on day 21 of gestation. Body weights were taken on days 0, 6, 9, 12, 15, 18 and 21 of gestation. Food consumption was evaluated for days 12 and 18 of gestation. Clinical observations were made daily for signs of pharmacologic or toxicologic effect and mortality. Gross necropsies were conducted on all surviving rats, moribund rats and rats that

died spontaneously. At necropsy, for rats sacrificed on day 13 of gestation, the uterus (number and location for each horn of resorptions, embryos and implantation sites) and ovaries (number of corpora lutea of pregnancy per ovary) were observed. At necropsy, for rats sacrificed on day 21 of gestation, the uterus (number and location for each horn of live fetuses, dead fetuses, early and late resorptions and implantation sites) and ovaries (number of corpora lutea of pregnancy per ovary) were observed. The necropsy for all maternal rats also included observations for obvious abnormalities and the following tissues were examined: heart, lung, stomach, liver, pancreas, spleen, mesenteric lymph nodes, jejunum, kidney, adrenal, bladder and ovary.

Results

Maternal toxicity NOEL:	> 500 mg/kg/day by gavage; > 475 mg/kg/day via diet
Developmental toxicity NOEL:	> 500 mg/kg/day by gavage; > 475 mg/kg/day via diet
Actual dose received:	100 or 500 mg/kg/day by gavage; 475 mg/kg/day via diet
Maternal data:	No adverse effects attributable to compound administration were noted in comparisons of pregnancy and mortality rates. One rat was found dead on test day 13; it was determined that she was pregnant. Early deliveries and abortions, necropsy findings, and reproduction data were considered not to be affected by treatment with the test substance. An increase in resorptions was observed for the 500 mg/kg/day gavage group compared to the isopropanol control group (8.9% vs 2.1%). This difference was not considered a treatment-related effect due to the lack of similar response in the diet-exposed group and a low value for the control group compared to historical data from the laboratory.
Fetal data:	No differences considered related to the administration of either test substance were noted in fetal size and sex, variations in degree of ossification or malformations.
Statistical results:	Described above
Remarks:	

Conclusions

Remarks:	The endpoint has been adequately characterized. (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2A

Remarks: Reliable with restrictions; acceptable, well-documented publication/study report which meets basic scientific principles.

References

Killeen, J. C., Jr. and W. R. Rapp. 1975. A Rat Teratology Study of XSA-201-202. Project number 73R-927. Bio/dynamics Inc.

Other

Last changed: December 13, 2001
Order number for sorting: 22a
Remarks:

5.10 ADDITIONAL REMARKS

Test Substance

Identity:	Dialkyl (octadecyl) dimethyl ammonium chloride (CAS RN 68391-05-9; Quaternary ammonium compounds, di-C12-18-alkyldimethyl, chlorides)
Purity:	Not stated
Remarks:	

Method

Method/guideline followed:	Not stated
Type:	Acute dermal metabolism
GLP:	Not stated
Year:	1977 (date of publication)
Species/Strain:	Rabbit/strain not stated
Sex:	Not stated
No. of animals per sex per dose:	4 rabbits per group
Vehicle:	None
Route of administration:	Dermal
Remarks:	Ten milligrams (~30 μCi) of [^{14}C] dialkyl (octadecyl) dimethyl ammonium chloride was applied to the back of each of four rabbits over a 5 x 8 cm area. The rabbits were then restrained for 72 hours so they could not lick the material from their backs or rub against their cages. Their excreta were collected over a 72-hour period and were assayed for radioactivity. The distribution of radioactivity between excreta, test skin site, untreated skin and the cage wash was determined.

Results

Remarks:	Total recovered ^{14}C after application of dioctadecyl dimethyl [1-^{14}C] ammonium chloride was 89%. Only traces of radioactivity were found in the carbon dioxide (0.27%), urine (0.15%), feces (0.16%), untreated skin (0.2%) and cage wash (0.29%). Most of the radioactivity was recovered from the skin site where it had been applied (88%).

Conclusions

Remarks:	Dialkyl (octadecyl) dimethyl ammonium chloride does not effectively penetrate the skin (Author of the article) The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions; a metabolism study with acute exposure.

References

Drotman, R. B. 1977. Metabolism of Cutaneously Applied Surfactants. pp. 95 - 109. In Cutaneous Toxicity. Academic Press Inc., New York, NY, U. S.

Other Available Reports

Other

Last changed:	December 13, 2001
Order number for sorting:	26
Remarks:	

5.10 ADDITIONAL REMARKS

Test Substance

Identity:	Dimethyl-di-"Hydrogenated Tallow" Ammonium Chloride (CAS RN 61789-80-8; Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chloride)
Purity:	Not stated
Remarks:	

Method

Method/Guideline followed:	Not stated
Test type:	Oral feed
GLP:	No
Year:	1971
Species:	Rat
Strain:	Not stated (only albino stated)
Route of administration:	Dietary
Duration of test:	90-days
Doses/concentration levels:	7, 140 and 2800 ppm
Sex:	Male and female
Exposure period:	90-days
Frequency of treatment:	Not stated
Control group and treatment:	Not stated
Postexposure observation period:	None
Statistical methods:	Not stated
Remarks:	Six rats (three males and three females) from each dose group were placed in metabolism cages to collect urine and feces over a 24-hour period. The samples were packaged separately, frozen then analyzed for quaternary content, using a colorimetric method. The recovery on spiked samples was around 80% in low ppm concentration ranges. With these data confirming the method, the samples were then analyzed. (It is not specifically stated in this report that these samples were taken at the end of the 90-day test period. It can only be assumed since they supply a value for the compound consumed.)

Results

NOAEL (NOEL):	Not applicable
LOAEL (LOEL):	Not applicable
Actual dose received:	During the last six weeks of the test: 7 ppm: Males = 0.4 mg/kg/day Females = 0.5 mg/kg/day 140 ppm: Males = 7.0 mg/kg/day Females = 10.0 mg/kg/day 2800 ppm: Males = 170.2 mg/kg/day Females = 221.6 mg/kg/day
Toxic response/effects:	Not stated
Statistical results:	None
Remarks:	The average recovery of Arquad from the urine and feces of the rats in the 2800 ppm group was 15.8% of the dose consumed for males and 6.0% for females. At the low levels (7 and 140 ppm) practically no quaternary in the excreta was recovered.

Conclusions

Remarks: From these data, one can conclude that appreciable amounts of the quaternary were metabolized by the animals. (Author of report)
The endpoint has been adequately characterized (American Chemistry Council Fatty Nitrogen Derivatives Panel, Cationics Task Group).

Data Quality

Reliability (Klimisch):	2D
Remarks:	Reliable with restrictions; this reports provides only the metabolism phase of the 90-day dietary rat study.

References

Metcalfe, L. D., R. J. Jakubiec and Chu-Nan Wang. 1971. A Short-Term Metabolic Study of Rats on a Diet Containing Dimethyl-di-“hydrogenated Tallow” Ammonium Chloride. Research Laboratories, Armour Industrial Chemical Company, McCook, IL, U. S.

Other

Last changed:	December 13, 2001
Order number for sorting:	20a
Remarks:	

Government Review Documents of
Alkyl (C12-16) Dimethylbenzylammonium Chloride (ADBAC; CAS RN 68424-85-1)
and Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5)

Appendix B

Government Review Documents of
Alkyl (C12-16) Dimethylbenzylammonium Chloride (ADBAC; CAS RN 68424-85-1)
and Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5)

1. U. S. EPA. 1997. Data Evaluation Report of:
   "Static-Renewal Acute Toxicity of ADBAC to Fathead Minnow (*Pimephales promelas*)." ABC Labs 41237 and 41237R. MRID #437401-03 (for Endpoint 4.1: Acute Toxicity to Fish); and

   "Static-Renewal Acute Toxicity of ADBAC to Fathead Minnow *(Pimephales promelas*) in Dilution Water Amended with 10 mg/L Humic Acid." ABC Labs 41235 and 41236R. MRID #437401-02 (for Endpoint 4.1: Acute Toxicity to Fish); and

   "Static-Renewal Acute Toxicity of ADBAC to Fathead Minnow (*Pimephales promelas*) in Dilution Water Amended with 20 mg/L Humic Acid." ABC Labs 41235 and 41235R. MRID #437401-01 (for Endpoint 4.1: Acute Toxicity to Fish).

2. U. S. EPA. 1993. Data Evaluation Report of:
   "Daily Static-Renewal Acute 96-Hour Toxicity Test of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) to Bluegill Sunfish." MRID #419472-01 and #429174-01 (for Endpoint 4.1: Acute Toxicity to Fish); and

   "Daily Static Renewal Acute 96-Hour Toxicity Test of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) to Rainbow Trout." MRID #419472-02 and 429174-02 (for Endpoint 4.1: Acute Toxicity to Fish); and

   "Daily Static Renewal Acute 48-Hour Toxicity Test of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) to *Daphnia magna*." MRID #419472-03 (for Endpoint 4.2: Acute Toxicity to Aquatic Invertebrates).

3. U. S. EPA. 1993. Data Evaluation Report of:
   "A 96-Hour Static-Renewal Acute Toxicity Test with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Sheepshead Minnow *(Cyprinodon variegatus*)." Project number 350-102. Wildlife International, Ltd., Easton, MD. MRID #424795-02 (for Endpoint 4.1: Acute Toxicity to Fish); and

   "A 96-Hour Static-Renewal Acute Toxicity Test with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Saltwater Mysid *(Mysidopsis bahia*)." Project number 350A-101A. Wildlife International, Ltd., Easton, MD. MRID #424795-01 (for Endpoint 4.2: Acute Toxicity to Aquatic Invertebrates); and

   "A 48-Hour Static Acute Toxicity Test with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Embryo Larvae of the Eastern Oyster (*Crassostrea virginica*)." MRID #424795-03 (for Endpoint 4.2: Acute Toxicity to Aquatic Invertebrates).

Government Review Documents of
Alkyl (C12-16) Dimethylbenzylammonium Chloride (ADBAC; CAS RN 68424-85-1)
and Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5)

4. U. S. EPA. 1997. Data Evaluation Report of:

"Daily Static-Renewal Early Life Stage Toxicity Test of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) to Fathead Minnows." Battelle study number SC890057. Battelle Columbus Operations, Columbus, OH. MRID #423021-02 (for Endpoint 4.5.1: Chronic Toxicity to Fish); and

"Daily Static-Renewal Chronic 21-Day Toxicity Test of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) to *Daphnia magna*." Battelle study number SC890056. Battelle Columbus Operations, Columbus, OH. MRID #423021-01 (for Endpoint 4.5.2: Chronic Toxicity to Aquatic Invertebrates).

5. U. S. EPA. 1989. Data Evaluation Report of "Ninety-Day Dietary Toxicity Study with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Rats." Laboratory project ID 51-503. Bushy Run Research Center, Export, PA. MRID #407466-01 (for Endpoint 5.4: Repeated Dose Toxicity).

6. U. S. EPA. 1993. Data Evaluation Report of "Evaluation of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Ninety-Day Subchronic Dermal Toxicity Study in Rats." Bushy Run Research Center, Export, PA. MRID #414996-01 (for Endpoint 5.4: Repeated Dose Toxicity).

7. U. S. EPA. 1993. Data Evaluation Report of "Evaluation of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Combined Chronic Toxicity/Oncogenicity Study in Rats." Bushy Run Research Center, Export, PA. MRID #419475-01 (for Endpoint 5.4: Repeated Dose Toxicity).

8. U. S. EPA. 1993. Data Evaluation Report of "Chronic Dietary Oncogenicity Study with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Mice." Bushy Run Research Center, Export, PA. MRID #417652-01 (for Endpoint 5.4: Repeated Dose Toxicity).

9. U. S. EPA. 1993. Data Evaluation Report of "Genotoxicity Test on Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Assay for Unscheduled DNA Synthesis in Rat Liver Primary Cell Cultures." Hazleton Washington Inc., Vienna, VA. MRID #422908-01 (for Endpoint 5.5: Genetic Toxicity *In Vitro*).

Government Review Documents of
Alkyl (C12-16) Dimethylbenzylammonium Chloride (ADBAC; CAS RN 68424-85-1)
and Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5)

10. U. S. EPA. 1989. Data Evaluation Report of:
"Mutagenicity Test on Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the CHO/HGPRT Forward Mutation Assay." Hazleton Laboratories American, Kensington, MD. MRID #410127-01 (for Endpoint 5.5: Genetic Toxicity *In Vitro*); and

"Assessment of the Mutagenic Activity of Hyamine-3500 in the Mouse Micronucleus Test." SCANTOX, Skensved, Denmark. MRID #403111-01 (for Endpoint 5.6: Genetic Toxicity *In Vivo*).

11. U. S. EPA. 1993. Data Evaluation Report of "Two-Generation Reproduction Study in Sprague-Dawley (CD®) Rats With Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Administered in the Diet." Bushy Run Research Center, Export, PA. MRID #413850-01 (for Endpoint 5.8: Toxicity to Reproduction).

12. U. S. EPA. 1992. Data Evaluation Report of "Developmental Toxicity Evaluation II of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Administered by Gavage to CD® Rats." Bushy Run Research Center, Export, PA. MRID #423515-01 and #426451-01 (for Endpoint 5.9: Developmental Toxicity/Teratogenicity).

13. U. S. EPA. 1992. Data Evaluation Report of "Developmental Toxicity Evaluation of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Administered by Gavage to New Zealand White Rabbits." Bushy Run Research Center, Export, PA. MRID #423928-01 and #427344-01 (for Endpoint 5.9: Developmental Toxicity/Teratogenicity).

14. Environment Canada. 1998. "Water Quality Guideline for the Protection of Freshwater Aquatic Life for Didecyl Dimethyl Ammonium Chloride (DDAC)." Hull, Quebec (Multiple Endpoints).

15. Ministry of Environment, Lands and Parks. 1992. "A Review of the Environmental Impact and Toxic Effects of DDAC." Victoria, British Columbia (Multiple Endpoints).

SCAN 1

RECEIVED FEB 13 1997

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FEB 6 1997

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

Jim T. Hill, Ph.D.
Director
Product Ingredient Review Program
for the ADBAC Joint Venture
Chemical Specialties Manufacturers Association
1913 Eye Street, N.W.
Washington, DC 20006

SUBJECT: Review of Acute Fathead Minnow Studies with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) (MRIDS - 437401-01; 437401-02; 437401-03) Guideline 72-1(a)

Dear Dr. Hill:

The Agency has completed it's review of the three acute toxicity studies submitted by the Chemical Specialties Manufacturers Association to support the reregistration of ADBAC. The following is a brief summary of the reviews:

1. "Static-Renewal Acute Toxicity of ADBAC to Fathead Minnow (<u>Pimephales promelas</u>) ABC Labs 41237 and 41237R.

   <u>CONCLUSION:</u> This study is scientifically sound but does not fulfill the guideline requirements for an acute fish toxicity test of ADBAC with warmwater fish **(Guideline 72-1(a); MRID 437401-03)** since the Fathead Minnow is not the preferred species. ADBAC is classified as highly toxic to fathead minnows.

2. "Static-Renewal Acute Toxicity of ADBAC to Fathead Minnow (<u>Pimephales promelas</u>) in Dilution Water Amended with 10 mg/L Humic Acid, ABC Labs 41235 and 41236R.

   <u>CONCLUSION:</u> This study is scientifically sound, but does not fulfill the guideline requirements for an acute fish toxicity test of ADBAC with warmwater fish **(Guideline 72-1(a); MRID 437401-02)** due to addition of humic acid to the dilution water and can be classified as **Supplemental.** With the presence of 10mg/L humic acid, ADBAC is considered highly toxic to fathead minnows.

3. "Static-Renewal Acute Toxicity of ADBAC to Fathead Minnow (Pimephales promelas) in Dilution Water Amended with 20 mg/L Humic Acid, ABC Labs 41235 and 41235R.

CONCLUSION: This study is scientifically sound but does not fulfill the guideline requirements for an acute fish toxicity test of ADBAC with warmwater fish **(Guideline 72-1(a), MRID #437401-01)** due to the addition of humic acid to the dilution water and can be classified as **Supplemental.** In the presence 20mg/L humic acid, ADBAC is considered moderately toxic to fathead minnows.

If you have any questions, please do not hesitate to contact Ms. Beverly Sjoblad at (703) 308-8376, Office of Pesticide Programs, Reregistration Division, Section II.

Sincerely,

Lawrence J. Schnaubelt

Lawrence J. Schnaubelt, Head
Registration Branch, Section II
Special Review and
Reregistration Division

Enclosures

DATA EVALUATION RECORD
§ 72-1(A) -- ACUTE LC_{50} TEST WITH A WARMWATER FISH

1. **CHEMICAL:** Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) PC Code No.: 069105

2. **TEST MATERIAL:** ADBAC Quat 80% (lot #7293k) Purity: 81.9 %
^{14}C-ADBAC (ABC Ref. #RS-6654 Purity: 98.4%

3. **CITATION**

Authors: Sword, Marc C., & Luke Stuerman
Title: Static-Renewal Acute Toxicity of ADBAC to Fathead Minnow (*Pimephales promelas*)
Study Completion Date: November 19, 1993
Laboratory: ABC Laboratories, Inc., Environmental Toxicology Division, 7200 E. ABC Lane, Columbia, Missouri 65202
Sponsor: ADBAC Quat Joint Venture/Chemical Specialties Manufacturers Association
Laboratory Report ID: ABC Laboratories' Study #41237
MRID No.: 437401-03
DP Barcode: D220177

4. **REVIEWED BY:** Harry A. Winnik, Biologist, EEB, EFED

Signature: **Date:** 3/18/96

5. **APPROVED BY:** Henry T. Craven, Head of Section #IV, EEB, EFED

Signature: Henry T. Craven **Date:** 3/18/96

6. **STUDY PARAMETERS**

Scientific Name of Test Organism: Fathead Minnow (*Pimephales promelas*)
Age or Size of Test Organism: Mean length: 18 ± 3mm Range: 15 - 26mm Weight: 0.08 ± 0.05 g
Definitive Test Duration: 96 hours
Study Method: Static-Renewal
Type of Concentrations: Mean measured

7. **CONCLUSIONS:**

Results Synopsis
LC_{50}: 0.28 ppm ai 95% C.I.: 0.23-0.34 ppm ai
NOEC: N/A Probit Slope: N/A

8. **ADEQUACY OF THE STUDY**

A. **Classification:** ~~Core~~ Supplemental

HTC
7/9/96

B. **Rationale:** This study is scientifically sound ~~and~~ but does not fulfill~~s~~ the guideline requirements for an acute fish toxicity test of ADBAC with warmwater fish (Guideling 72-1(a)

C. **Repairability:** N/A

9. **GUIDELINE DEVIATIONS**

There were no major guideline deviations in this study except that the fathead minnow is not the preferred species.

HTC
7/9/96

SCAN

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN

1-25-94

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Mr. Ralph Engel
Chemical Specialties Manufactures Association
1913 Eye St. N.W.
Washington, D.C. 20006

SUBJECT: Reregistration of Alkyl dimethyl ammonium chloride (ADBAC)
Acute toxicity - bluegill sunfish (gdln. 72-1a)
mrid 41947201 & 42917401
Acute toxicity - rainbow trout (gdln. 72-1c)
mrid 41947202 & 42917402
Acute invertebrate toxicity - *Daphnia magna* (gdln 72-2a)
mrid 41947203

Dear Mr. Engel:

We have reviewed the data cited above submitted to support the reregistration of ADBAC. The studies are acceptable and fulfill our guideline requirements. The LC_{50} or EC_{50} based on the acceptable data are as follows:

- *Lepomis macrochirus* LC_{50} = 515 µg/l (Bluegill Sunfish);
- *Oncorhynchus mykiss* LC_{50} = 923.2 µg/l (Rainbow Trout); and
- *Daphnia magna* EC_{50} = 5.9 µg/l (invertebrate).

Please refer to the enclosed Data Evaluation Records (DERs) for additional information.

If you have any questions or require additional information, please contact Ms. Brigid Lowery, the ADBAC Review Manager on (703) 308-8053.

Sincerely,

Lawrence J. Schnaubelt

Lawrence J. Schnaubelt, Section Head
Reregistration Branch, Section II
Special Review and
Reregistration Division

cc: John Lee (RD)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

NOV 30 1993

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

To: Larry Schnaubelt 72/Brigid Lowery
Special Review and Reregistration Division
7508W

From: Anthony F. Maciorowski, Chief
Ecological Effects Branch
7507C

for Douglas J. Urban 11/30/93

Subject: Review of Studies for ADBAC

The following studies were submitted as part of the reregistration process for ADBAC (067105):

Pate, H.O. and D.O. McIntyre, 1991. Daily Static Renewal Acute 96-Hour Toxicity Test of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) to Bluegill Sunfish. MRID No. 419472-01.

Pate, H.O. and D.O. McIntyre, 1991. Daily Static Renewal Acute 96-Hour Toxicity Test of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) to Rainbow Trout. MRID No. 419472-02.

Pate, H.O. and D.O. McIntyre, 1991. Daily Static Renewal Acute 48-Hour Toxicity Test of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) to Daphnia magna. MRID No. 419472-03.

Review Summary

Guide. Ref. No.	MRID No.	Test Type	Test Species	% ai	Test Results	Study Status
72-1 (a)	419472 -01	Static Acute Toxicity	*Lepomis macrochirus*	30	LC50 = 515 µg ai/l	Core
72-1 (c)	419472 -02	Static Acute Toxicity	*Oncorhynchus mykiss*	30	LC50 = 923.2 µg/l	Core
72-2 (a)	419472 -03	Static Acute Toxicity	*Daphnia magna*	95-96	EC50 = 5.9 µg/l	Core

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

August 11, 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of Estuarine Acute Toxicity Studies Submitted to Support Reregistration of Alkyl dimethyl benzyl ammonium chloride (ADBAC), Shaughnessy #069105.

FROM: Anthony F. Maciorowski, Chief
Ecological Effects Branch
Environmental Fate and Effects Division (H7507C)

8/19/93

TO: Brigid Lowery
Reregistration Branch
Special Review and Reregistration Division(H7508W)

EEB has completed review of three Estuarine Acute Toxicity Studies submitted by ADBAC Quat Joint Venture to support the reregistration of Alkyl dimethyl benzyl ammonium chloride (ADBAC), Shaughnessy #069105. (copies are attached). The following are brief summaries of the reviews:

CITATION: Sved, D.W., J.P. Swigert, and G.J. Smith. 1992. A 96-Hour Static-Renewal Acute Toxicity Test with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Saltwater Mysid (*Mysidopsis bahia*). Project No. 350A-101A. Prepared by Wildlife International Ltd., Easton, MD. Submitted by ADBAC Quat Joint Venture/Chemical Specialties Manufacturers Association, Washington, D.C. EPA MRID No. 424795-01.

CONCLUSIONS: This study is scientifically sound and meets the guideline requirements for an acute estuarine shrimp toxicity study (this study is classified as "core"). The 96-hour LC_{50} value was 0.092 ppm mean measured concentration. Therefore, ADBAC QUAT is classified as very highly toxic to mysids. The NOEC was 0.047 ppm.

RECOMMENDATIONS: N/A.

CITATION: Sved, D.W., J.P. Swigert, and G.J. Smith. 1992. A 96-Hour Static-Renewal Acute Toxicity Test with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Sheepshead Minnow (*Cyprinodon variegatus*). Project No. 350A-102. Prepared by

Wildlife International Ltd., Easton, MD. Submitted by ADBAC Quat Joint Venture/Chemical Specialties Manufacturers Association, Washington, D.C. EPA MRID No. 424795-02.

CONCLUSIONS: This study is scientifically sound and meets the guideline requirements for an acute estuarine fish toxicity study (this study is classified as "core"). The 96-hour LC_{50} value was 0.86 ppm mean measured concentration. Therefore, ADBAC QUAT is classified as highly toxic to sheepshead minnows. The NOEC was 0.68 ppm.

RECOMMENDATIONS: N/A.

CITATION: Sved, D.W., J.P. Swigert, and G.J. Smith. 1992. A 48-Hour Static Acute Toxicity Test with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Embryo Larvae of the Eastern Oyster (*Crassostrea virginica*). Project No. 350A-103. Prepared by Wildlife International Ltd., Easton, MD. Submitted by ADBAC Quat Joint Venture/Chemical Specialties Manufacturers Association, Washington, D.C. EPA MRID No. 424795-03.

CONCLUSIONS: This study is not scientifically sound (this study is classified as "invalid"). Control mortality (47.8%) was unacceptably high. Based on normalized embryo-larvae mortality, the 48-hour LC_{50} was 55.0 ppb mean measured concentration. Based on abnormal development, the 48-hour EC_{50} was 49.1 ppb mean measured concentration. Therefore, ADBAC QUAT is classified as very highly toxic to eastern oysters. The NOEC was 25.0 ppb.

RECOMMENDATIONS: N/A

If you have any questions regarding this submission please contact Harry Winnik, Biologist, 305-7089.

MRID No. 424795-01

DATA EVALUATION RECORD

1. **CHEMICAL:** Alkyl Dimethyl Benzyl Ammonium Chloride
Shaughnessey No. 069105.

2. **TEST MATERIAL:** 1) ADBAC QUAT 80%; Lot No. 7293K, CP-161-1, 010 0879; 80.8% active ingredient; a yellow clear liquid. 2) ADBAC (^{14}C); Lot No. 920326; 12.62 µCi/ml; 97.99-98.74% radiochemical purity; a clear colorless liquid.

3. **STUDY TYPE:** 72-3. Estuarine Shrimp Static-Renewal Acute Toxicity Test. Species Tested: Mysid (*Mysidopsis bahia*).

4. **CITATION:** Sved, D.W., J.P. Swigert, and G.J. Smith. 1992. A 96-Hour Static-Renewal Acute Toxicity Test with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Saltwater Mysid (*Mysidopsis bahia*). Project No. 350A-101A. Prepared by Wildlife International Ltd., Easton, MD. Submitted by ADBAC Quat Joint Venture/Chemical Specialties Manufacturers Association, Washington, D.C. EPA MRID No. 424795-01.

5. **REVIEWED BY:**

Louis M. Rifici, M.S.
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: Louis M. Rifici
Date: 10/21/92

8-10-93

6. **APPROVED BY:**

Pim Kosalwat, Ph.D.
Senior Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: P. Kosalwat
Date: 10/21/92

Henry T. Craven, M.S.
Supervisor, EEB/EFED
USEPA

Signature: H.T. Craven 8/12/93
Date:

7. **CONCLUSIONS:** This study is scientifically sound and meets the guideline requirements for an acute estuarine shrimp toxicity study. The 96-hour LC_{50} value was 0.092 ppm mean measured concentration. Therefore, ADBAC QUAT is classified as very highly toxic to mysids. The NOEC was 0.047 ppm.

8. **RECOMMENDATIONS:** N/A.

9. **BACKGROUND:**

RECEIVED FEB 13 1997

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FEB 10 1997

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

Jim T. Hill, Ph.D.
Director
Product Ingredient Review Program
Chemical Specialties Manufactures Assn., Inc.
1913 Eye Street, N.W.
Washington, DC 20006

SUBJECT: Upgrade of Previously Reviewed Daphnia magna Life Cycle and Fish Early Life Stage Studies.

Dear Dr. Hill:

The Agency has completed its review of the information to support the upgrade of the previously reviewed Daphnia magna Life Cycle and Fish Early Life Stage studies and has come to the following conclusions:

Daphnia magna Life Cycle Study

The Agency agrees that both the original 9-day dose range-finding study and the definitive 21-day life cycle study were found to be scientifically sound, but were classified as supplemental due to the lack of information that would allow classification as Core. A supplemental classification does not mean that the study is invalid. **As such, the study will not be upgraded and retains the supplemental classification.** However, although the current information can not be used to upgrade the original definitive study, it can be used in a risk assessment and based on the current use patterns for ADBAC, the study will not have to be repeated at this time. (SEE ATTACHED MEMO.)

Fish Early Life Stage Study

The agency accepts the arguments presented by you regarding the feeding regime used in the Fish Early Life Stage study. Based on the information submitted, the Agency hereby upgrades the classification of the Freshwater Fish Early Life-Stage Test (MRID 423021-02) to CORE.

If you have any questions concerning this letter, please do not hesitate to contact Ms. Beverly Lavis at (703) 308-8376, Office of Pesticide Programs, Special Review and Registration Division, Reregistration Branch, Section II.

Sincerely,

Lawrence J. Schnaubelt

Lawrence J. Schnaubelt, Head
Reregistration Branch, Section II
Special Review and
Reregistration Division

Enclosure

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

March 20, 1996

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of Information Submitted to Support the Upgrade of Previously Reviewed *Daphnia magna* Life Cycle and Fish Early Life Stage Studies.

FROM: Anthony F. Maciorowski, Chief
Ecological Effects Branch
Environmental Fate and Effects Division (7507C)

N Cook for
04/02/96

TO: Larry Schnaubelt (PM 72)
Reregistration Branch
Special Review and Reregistration Division (7508W)

EEB has reviewed the information submitted to support the upgrade of the previously Reviewed *Daphnia magna* Life Cycle and Fish Early Life Stage Studies and has come to the following conclusions.

Daphnia magna Life Cycle Study[1]

EEB agrees with the registrant that both the 9-day dose range-finding study and the definitive 21-day life cycle study were scientifically sound. In fact, when the 21-day study was originally reviewed (DP barcode D179742, Oct. 2, 1992) it was considered scientifically sound and was classified as supplemental. A supplemental classification does not mean that the study was invalid. What it means is that although the study was scientifically sound it lacks the information that would allow classification as core. In this case, an MATC could not be determined from the definitive study. We cannot use information from a separate study to upgrade the original definitive study. As such, the study will not be upgraded and retains the supplemental classification. The information from the definitive study can be used in a risk assessment and based on the current use ~~information~~ patterns for ADBAC (SHA# 069105), the study will not have to be repeated at this time.

Fish Early Life Stage Study[2]

EEB accepts the arguments presented by the registrant regarding the feeding regime used in the Fish Early Life Stage study. Based on the information submitted EEB hereby upgrades the classification of the Freshwater Fish Early Life-Stage Test (MRID 423021-02) to CORE. Based on mean measured concentrations, the NOEC and LOEL for *Pimephales promelas* were 32.2 and 75.9 $\mu g/l$. The MATC was calculated to be 49.4 $\mu g/l$.

1. McIntyre, D.O. and H.O. Pate, 1992, Daily Static-Renewal Chronic 21-Day Toxicity Test of Alkyl dimethyl Benzyl Ammonium Chloride (ADBAC) to *Daphnia magna*, Batelle Study No. SC890056, conducted by Batelle Columbus Operations, Columbus, OH, submitted by ADBAC Quat Joint Venture/Chemical Specialties Manufacturers Association, Washington, D.C., EPA MRID No. 423021-01.

2. McIntyre, D.O. and H.O. Pate, 1992, Daily Static-Renewal Early Life Stage Toxicity Test of Alkyl dimethyl Benzyl Ammonium Chloride (ADBAC) to Fathead Minnows, Batelle Study No. SC890057, conducted by Batelle Columbus Operations, Columbus, OH, submitted by ADBAC Quat Joint Venture/Chemical Specialties Manufacturers Association, Washington, D.C., EPA MRID No. 423021-02.

COPY

MRID No. 423021-02

DATA EVALUATION RECORD

1. **CHEMICAL:** Alkyl dimethyl benzyl ammonium chloride (ADBAC). Shaughnessey No. 069105.

2. **TEST MATERIAL:** 1) ^{14}C-alkyl dimethyl benzyl ammonium chloride (ADBAC); 25 mCi/mmole; 98.4% radiopurity; a clear liquid. 2) Non-radiolabelled ADBAC; ADBAC Quat/Lot No. 05-6K, BTC 835; 30% active ingredient; a clear yellowish liquid.

3. **STUDY TYPE:** 72-4. Freshwater Fish Early Life-Stage Test. Species Tested: Fathead Minnow (*Pimephales promelas*).

4. **CITATION:** McIntyre, D.O. and H.O. Pate. 1992. Daily Static-Renewal Early Life Stage Toxicity Test of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) to Fathead Minnows. Battelle Study No. SC890057. Conducted by Battelle Columbus Operations, Columbus, OH. Submitted by ADBAC Quat Joint Venture/Chemical Specialties Manufacturers Association, Washington, D.C. EPA MRID No. 423021-02.

5. **REVIEWED BY:**

Rosemary Graham Mora, M.S.
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: P. Kosalwat for RGM

Date: 9/15/92

6. **APPROVED BY:**

Pim Kosalwat, Ph.D.
Senior Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: P. Kosalwat

Date: 9/15/92

Henry T. Craven, M.S.
Supervisor, EEB/EFED
USEPA

Signature: Henry T Craven

Date: Concepcion Rodriguez 9/30/92 9/30/92

7. **CONCLUSIONS:** This study is scientifically sound but does not fulfill the guideline requirements for a fish early life-stage toxicity test. It appears that the fish were not fed at the same rate (g food/fish) in all chambers; consequently, the food appears to be a limiting factor in this test. Based on mean measured concentrations, the MATC for *Pimephales promelas* was >32.2 and <75.9 μg/l ADBAC (geometric mean MATC = 49.4 μg/l).

8. **RECOMMENDATIONS:**

16E

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

007287

JUN 29 1989

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC)

TO: John Lee PM-31
Registration Division (H7505C)

6/15/89

FROM: Robert P. Zendzian ~~Ph.D.~~,
Acting Head, Rev Sec I
Toxicology Branch I
Health effects Division (H7509C)

THROUGH: Edwin Budd
Acting Chief
Toxicology Branch I

Budd 6/22/89

Compound; ADBAC Tox Chem #016 16E Registration #069105

Registrant; CSMA/ADBAC Quat Joint Venture MRID # 407466-01

Tox Project #9-0901

Action Requested

Review the following study submitted in reply to a Registration Standard;

Ninety-day dietary toxicity study with Alkyl Dimethyl Benzyl Ammonium Choloride (ADBAC) in rats, J.P. Van Miller & E.V. Weaver; Union Carbide, Bushy Run Research Center; Lab Project ID # 51-503; June 20 ,1988; MRID # 407466-01.

Conclusion

Core Classification Minimum

Sprague-Dawley rats were dosed with ABDAC at 0, 100, 500, 1000, 4000 and 8000 ppm in the diet. Compound was lethal at doses of 4000 and 8000 ppm. At 1000 ppm decreased body weight gain with no effect on food consumption was observed in the males. No other toxic effects were observed. LEL=1000 ppm, NOEL=500 ppm.

Attachment

DER

EPA No.: 68D80056
DYNAMAC No.: 164-B
TASK No.: 1-64B
May 25, 1989

DATA EVALUATION RECORD

ALKYL DIMETHYL
BENZYL AMMONIUM CHLORIDE

Subchronic Toxicity Feeding Study in Rats

APPROVED BY:

Robert J. Weir, Ph.D.
Program Manager
Dynamac Corporation

Signature: Robert J. Weir

Date: May 25, 1989

EPA No.: 68D80056
DYNAMAC No.: 164-A
TASK No.: 1-64A
May 25, 1989

DATA EVALUATION RECORD

ALKYL DIMETHYL BENZYL AMMONIUM CHLORIDE

Subchronic Toxicity Feeding Study in Rats

<u>REVIEWED BY</u>:

William L. Richards, Ph.D.
Principal Reviewer
Dynamac Corporation

Signature: William L. Richards
Date: May 25, 1989

Margaret E. Brower, Ph.D.
Independent Reviewer
Dynamac Corporation

Signature: Margaret E. Brower
Date: May 25, 1989

<u>APPROVED BY</u>:

Roman J. Pienta, Ph.D.
Department Manager
Dynamac Corporation

Signature: Roman J Pienta
Date: May 25 1989

William Burnam, M.S.
EPA Reviewer and
Acting Chief,
Herbicide/Fungicide/
Antimicrobial Support
Toxicology Branch II (H-7509C)

Signature: Wm F Burnam
Date: 7/10/89

DATA EVALUATION RECORD

STUDY TYPE: Subchronic toxicity feeding study in rats. GUIDELINE §82-1

MRID NUMBER: 407466-01.

TEST MATERIAL: Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC).

SYNONYM(S): Benzalkonium chloride, Zephiran chloride, Zephirol, BTC, Roccal, Benirol, Enuclen, Germitol, Drapolene, Drapolex, Cequartyl, Paralkan, Germinol, Rodalon, Osvan.

STUDY NUMBER(S): Laboratory Project ID 51-503.

SPONSOR: ADBAC QUAT Joint Venture/Chemical Specialties Manufacturers Association, Washington, D.C.

TESTING FACILITY: Bushy Run Research Center, Export, PA.

TITLE OF REPORT: Ninety-Day Dietary Toxicity Study with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Rats.

AUTHOR(S): J. P. Van Miller and E. V. Weaver.

REPORT ISSUED: June 20, 1988.

CONCLUSIONS:

When ADBAC was fed to Sprague-Dawley rats for up to 95 (males) or 96 (females) days at dietary concentrations of 0, 100, 500, 1000, 4000, or 8000 ppm, evidence of severe toxicity was observed in rats of both sexes in the 4000- and 8000-ppm groups. All of the rats in the 8000-ppm group died from day 4 to day 8 of the study; in the 4000-ppm groups, 12/15 males died from day 7 to day 19 and 11/15 females died from day 7 to day 11. Other compound-related findings in the 4000- and 8000-ppm groups included cachexia (emaciation, body thinness), loose feces, decreased body weight, and body weight gain, decreased food consumption, decreased organ weights in males (liver, kidneys, spleen, and heart), gross lesions (intestinal ileus consisting of distended fluid- and gas-filled viscera extending from the stomach to the cecum, perineal staining, decreased spleen size, brain hemorrhage, and color change in the lungs), and nonneoplasic histologic lesions [stomach congestion and edema, stomach hemorrhage (only in males), congestion of the small intestine and cecum; mucosal cell degeneration in the duodenum, jejunum (only in males), ileum (only in males), and cecum (only in males), congestion and hepatocellular atrophy in the liver, contracted spleen, brain congestion, and congestion and hemorrhage of the lungs]. Except for a slightly earlier time of death in females in the 8000-ppm group than in males in that group, signs and symptoms of compound-related toxicity, especially nonneoplastic histologic lesions, tended to be more marked in males than females in the 4000- and 8000-ppm groups. Gross pathologic findings and microscopic lesions supported ileus, hypovolemic shock, hemorrhage of the brain and lungs, and, perhaps, brain and liver congestion as the probable cause of death. Changes in serum glucose and phosphorus levels were in the normal range of variation for this rat strain. Slight elevations in SGPT and SGOT activities may have been related to stress. At the lower dietary concentrations (1000, 500, and 100 ppm), the only clearly compound-related findings were decreased body weight and decreased body weight gain, with no effect on food consumption, in males of the 1000-ppm group during part of the period of compound administration. No treatment-related changes were observed in any hematology measurement or in the ophthalmologic examination. Based on the effects of ADBAC on body weight at 1000 ppm, the Lowest-Observed-Effect Level (LOEL) is 1000 ppm, and the No-Observed-Effect Level (NOEL) is 500 ppm.

Classification: Core Minimum (see Reviewers' Discussion and Interpretation of Results).

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUL 2 8 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Evaluation of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Ninety-Day Subchronic Dermal Toxicity Study in Rats. Guideline Series 82-3. (MRID 414 996-01)

Tox Chem No.: 016E
EPA ID No.: 069105
DP Barcode No.: D167282
Submission No.: S400536
Case No.: 819070

FROM: Brian Dementi, Ph.D., D.A.B.T. Brian Dementi 7/15/93
Review Section III
Toxicology Branch I
Health Effects Division (H7509C)

TO: Brigid Lowery, PM Team 72
Reregistration Branch
Special Review and Reregistration Division (H7508W)

THRU: Karen Hamernik, Ph.D. KB 7/20/93
Section Head, Review Section III
Toxicology Branch I
Health Effects Division (H7509C) K. Hamernik 7/16/93

The Data Evaluation Review for the ADBAC 90-day subchronic dermal toxicity study, submitted by Chemical Specialties Manufacturers Association toward satisfying the Registration Guideline Series 82-3 testing requirement is herewith submitted to SRRD.

Results of this study are summarized as follows. For further details see the Data Evaluation Review.

The test material as evaluated by the dermal route of administration for 90 days in 15 rats/sex/dose-group at dosage levels of 0, 2, 6 or 20 mg/kg/day did not elicit any toxicological effects that could be ascribed to the test material.

Please be advised that the study is rated Core Supplementary, the reason being that a LOEL was not identified under circumstances where the doses employed were too far below the limit dose.

DOC 920182

FINAL

DATA EVALUATION REPORT

Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC)

Study Type: Subchronic Dermal Toxicity in Rats

Prepared for:

Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by:

Clement International Corporation
9300 Lee Highway
Fairfax, VA 22031-1207

August 17, 1992

Principal Author ____ Date 8/17/92
Carrie Rabe, Ph.D.

Reviewer ____ Date 8-17-92
Wayne Reichardt, M.S.

QA/QC Manager ____ Date 8/17/92
Sharon Segal, Ph.D.

Contract Number: 68D10075
Work Assignment Number: 1-51
Clement Number: 91-165
Project Officer: James E. Scott

Guideline Series 82-3: Subchronic Dermal Toxicity in the Rat

EPA Reviewer: Brian Dementi, Ph.D.
Review Section III, Toxicology Branch I
Health Effects Division

Signature: Brian Dementi
Date: 8/26/92

EPA Acting Section Head:
Karen Hamernik, Ph.D., Review Section III,
Toxicology Branch I, Health Effects Division

Signature: Karl P. Baetcke for
Date: 2/23/93

DATA EVALUATION REPORT

STUDY TYPE: Subchronic dermal toxicity in rats

TEST MATERIAL: Alkyl dimethyl benzyl ammonium chloride (ADBAC)

Tox. Chem. Number: 016E

P.C. Number: 069105

SYNONYMS: Benzalkonium chloride

CAS Number: 68391-01-5

STUDY NUMBER: 52-623

MRID Number: 414996-01

SPONSOR: ADBAC QUAT Joint Venture/
Chemical Specialties Manufacturers Association
1913 Eye Street, N.W.
Washington, D.C. 20006

TESTING FACILITY: Bushy Run Research Center
6702 Mellon Road
Export, PA 15632

TITLE OF REPORT: Ninety-Day Subchronic Dermal Toxicity Study with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Rats

AUTHORS: M.W. Gill and C.L. Wagner

REPORT ISSUED: Completion date, May 14, 1990

CONCLUSIONS: Application of ADBAC, at dose levels of 2, 6, and 20 mg/kg/day, to the clipped backs of Sprague-Dawley rats for 6-8 hours/day, 5 days/week, for 13 weeks was associated with no toxicological effects that could be definitively attributed to the test material. The NOELs for dermal and systemic toxicity were 20 mg/kg/day.

CORE CLASSIFICATION: This study is classified as Core Supplementary because LOELs were not achieved for either dermal or systemic toxicity. The doses used were far below the limit dose.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUL 26 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Evaluation of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Combined Chronic Toxicity/Oncogenicity Study in Rats. Guideline Series 83-5. (MRID 419475-01)

Tox Chem No.: 016E
EPA ID No.: 069105
DP Barcode No.: D167336
Submission No.: S400617
Case No.: 819070

FROM: Brian Dementi, Ph.D., D.A.B.T. Brian Dementi 7/15/93
Review Section III
Toxicology Branch I
Health Effects Division (H7509C)

TO: Brigid Lowery, PM Team 72
Reregistration Branch
Special Review and Reregistration Division (H7508W)

THRU: Karen Hamernik, Ph.D.
Section Head, Review Section III
Toxicology Branch I
Health Effects Division (H7509C) K. Hamernik 7/16/93 KB 7/20/93

The Data Evaluation Review for the ADBAC combined chronic toxicity/oncogenicity study in rats, submitted by Chemical Specialties Manufacturers Association toward satisfying the Registration Guideline Series 83-5 testing requirement is herewith submitted to SRRD.

The test material was evaluated in the Sprague-Dawley rat via the dietary route of administration for two years at dosage levels of 0, 300, 1000 and 2000 ppm. There was no evidence of carcinogenicity under the conditions of the study. With respect to systemic toxicity, LOEL = 2000 ppm (decreased body weight, body weight gain and food consumption); NOEL = 1000 ppm. The study is rated Core Minimum. For further details please see the Data Evaluation Review with attached Addendum regarding dose selection issue.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Addendum to the Clement Data Evaluation Review for the combined chronic/oncogenicity study of ADBAC in the rat: dose selection issue. (MRID 419475-01)

FROM: Brian Dementi, Ph.D., D.A.B.T. Brian Dementi 5/4/93
Review Section III
Toxicology Branch I
Health Effects Division (H7509C)

Karl Baetcke 5/4/93

TO: ADBAC File
(RETAIN WITH DER)

In order to validate that 2000 ppm ADBAC was an MTD, the 90-day and 14-day range finding studies cited in the study were visited. The 90-day study, which evaluated doses of 0, 100, 500, 1000, 4000 and 8000 ppm, clearly revealed excessive mortality at 4000 and 8000 ppm. There was no clear dose related toxicity apparent at the lower doses. We should note the steep dose response for mortality. The 14-day study followed with doses of 0, 2000 and 3000 ppm. There was no mortality at any dose. Toxic signs at 3000 ppm included 100% incidence of loose feces, decreased food consumption and decreases in body weight. Also observed were excessive intestinal fluid and gas. At 2000 ppm slight changes in food consumption and body weight were observed. Gas filled ceca remained a problem of some degree.

The Registrant's representatives visited the Agency in February 1988 to discuss dose selection based upon findings in the above studies. The Registrant initially proposed doses of 0, 300, 1000 and 2500 ppm for the 2-year study. Agency representatives suggested a high dose of 1000-2000 ppm. The Registrant subsequently elected to go with doses of 0, 300, 1000 and 2000 ppm.

In view of findings in the various studies, including the 2-year study itself, and deliberations that preceeded dose selection, it would appear that doses for the definitive study of 0, 300, 1000 and 2000 ppm were properly chosen and that an MTD was achieved.

[D167336]
Tox Chem No: 016E
PC Code : 069105

DOC 930061
FINAL

DATA EVALUATION REPORT

Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC)

Study Type: Combined Chronic Toxicity/Oncogenicity in Rats

Prepared for:

Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by:

Clement International Corporation
9300 Lee Highway
Fairfax, VA 22031-1207

August 17, 1992

Principal Author [signature] Carrie Rabe, Ph.D. Date 8/17/92

Reviewer [signature] Wayne Reichardt, M.S. Date 8-17-92

QA/QC Manager [signature] Sharon Segal, Ph.D. Date 8/17/92

Contract Number: 68D10075
Work Assignment Number: 1-51
Clement Number: 91-168
Project Officer: James E. Scott

EPA Reviewer: Brian Dementi, Ph.D.
Review Section III, Toxicology Branch I
Health Effects Division

Signature: Brian Dementi
Date: 8/20/92

EPA Acting Section Head:
Karen Hamernik, Ph.D., Review Section III
Toxicology Branch I, Health Effects Division

Signature: [illegible]
Date: 7/8/93

DATA EVALUATION REPORT

STUDY TYPE: Combined chronic toxicity/oncogenicity in rats

TEST MATERIAL: Alkyl dimethyl benzyl ammonium chloride (ADBAC)

TOX. CHEM. NUMBER: 016E   P.C. NUMBER: 069105

SYNONYMS: Benzalkonium chloride   CAS Number: 68391-01-5

STUDY NUMBER: 53-543   MRID NUMBER: 419475-01

SPONSOR: ADBAC QUAT Joint Venture/
Chemical Specialties Manufacturers Association
1913 Eye Street, N.W.
Washington, D.C. 20006

TESTING FACILITY: Bushy Run Research Center
6702 Mellon Road
Export, PA 15632

TITLE OF REPORT: Chronic Dietary Toxicity/Oncogenicity Study with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Rats

AUTHORS: M.W. Gill, S.J. Hermansky, and C.L. Wagner

REPORT ISSUED: Completion date, July 8, 1991

CONCLUSIONS: ADBAC was administered via the diet to Sprague-Dawley rats for 104 weeks at doses of 0, 300, 1,000, and 2,000 ppm. The average daily intake values of ADBAC at these dietary levels were 13, 44, and 88 mg/kg/day for males and 17, 57, and 116 mg/kg/day for females. ADBAC was not oncogenic under the conditions of this study. Systemic toxicity, as indicated by decreased body weight, body weight gain, and food consumption, occurred with a LOEL of 2,000 ppm and a NOEL of 1,000 ppm. The following treatment related effects were observed:

300 ppm -- Equivalent to 13 mg/kg/day in males and 17 mg/kg/day in females. No treatment-related effects were observed.

1,000 ppm -- Equivalent to 44 mg/kg/day in males and 57 mg/kg/day in females. No treatment-related toxicity was observed.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUL 28 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Evaluation of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in an Oncogenicity Study in Mice. Guideline Series 83-2. (MRID 41765 2-01)

Tox Chem No.: 016E
EPA ID No.: 069105
DP Barcode No.: D166029
Submission No.: S398755
Case No.: 819070

FROM: Brian Dementi, Ph.D., D.A.B.T. Brian Dementi 7/15/93
Review Section III
Toxicology Branch I
Health Effects Division (H7509C)

TO: Brigid Lowery, PM Team 72
Reregistration Branch
Special Review and Reregistration Division (H7508W)

THRU: Karen Hamernik, Ph.D. K. Hamernik 7/16/93 KB 7/20/93
Section Head, Review Section III
Toxicology Branch I
Health Effects Division (H7509C)

The Data Evaluation Review for the ADBAC oncogenicity study in mice, submitted by the Chemical Specialties Manufacturers Association toward satisfying the Registration Guideline Series 83-2 testing requirement is herewith submitted to SRRD.

The test material was evaluated in CD-1 mice via the dietary route of administration for 78 weeks at dosage levels of 0, 100, 500 and 1500 ppm. There was no evidence of carcinogenicity under the conditions of the study. With respect to systemic toxicity, LOEL = 1500 ppm (decreased body weight and body weight gain); NOEL = 500 ppm. The study is rated Core Guideline. For further details please see the Data Evaluation Review.

Doc930062

FINAL

DATA EVALUATION REPORT

ADBAC

Study Type: Oncogenicity in Mice

Prepared for:

Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by:

Clement International Corporation
9300 Lee Highway
Fairfax, VA 22031-1207

March 30, 1992

Principal Author: John Liccione, Ph.D. Date 8/26/92

Reviewer: Wayne Reichardt, Ph.D. Date 8-26-92

QA/QC Manager: Sharon Segal, Ph.D. Date 8/26/92

Contract Number: 68D10075
Work Assignment Number: 1-51
Clement Number: 91-167
Project Officer: Mr. James Scott

EPA Reviewer: Brian Dementi, Ph.D.
Review Section III, Toxicology Branch I,
Health Effects Division

Signature: Brian Dement
Date: 8/31/92

EPA Acting Section Head: Karen Hamernik, Ph.D.
Review Section III, Toxicology Branch I,
Health Effects Division

Signature: K. [illegible] for
Date: 4/26/93

DATA EVALUATION REPORT

STUDY TYPE: Guideline Series 83-2: Chronic dietary oncogenicity study in mice.

TEST MATERIAL: Alkyl dimethyl benzyl ammonium chloride

MRID Number: 417652-01

SYNONYM: ADBAC

STUDY NUMBER: 53-515

SPONSOR: ADBAC QUAT Joint Venture/Chemical Specialties Manufacturers Association, 1913 Eye Street, N.W., Washington, D.C., 20006

TESTING FACILITY: Bushy Run Research Center, 6702 Mellon Road, Export, PA, 15632-8902

TITLE OF REPORT: Chronic Dietary Oncogenicity Study with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in Mice

AUTHORS: M.W. Gill, S.J. Hermansky, and C.L. Wagner

REPORT ISSUED: January 9, 1991

QUALITY ASSURANCE: A quality assurance statement was signed and dated January 8, 1991.

CONCLUSIONS: ADBAC was fed to male and female CD-1 mice at dietary levels of 0, 100, 500, or 1500 ppm. Mean body weights and body weight gains in the high-dose males and females were significantly lower than those of controls throughout most of the study. There was no significant effect of dosing on clinical signs, mortality, hematology, clinical chemistry, food consumption, gross pathology, or histopathology. ADBAC was not oncogenic under the conditions of the study.

The maximum tolerated dose (MTD) was reached in males and females. The LOEL is 1500 ppm based on decreases in body weights and body weight gains in males and females. The NOEL is 500 ppm.

Reviewed by: Irving Mauer, Ph.D., Geneticist 03-19-93
Toxicology Branch-I, HED (H7509C)
Secondary Reviewer: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch-I, HED (H7509C) 4/13/93

DATA EVALUATION RECORD

MRID NUMBER No.: 422908-01
PC No.: 069105
RD Record No.: S425912
EPA ID No.: 069105
Tox Chem. No.: 016I
Project No.: D182923

I. SUMMARY

STUDY TYPE: (84-4) Mutagenicity -- DNA damage/repair *in vitro* (HPC/UDS)

CHEMICAL: ADBAC [alkyl dimethyl benzyl ammonium chloride]

SPONSOR: ADBAC Quat Joint Venture/CSMA, Washington, D.C.

TESTING FACILITY: Hazleton Washington (HWA) Inc., Vienna, VA

TITLE OF REPORT: Genotoxicity Test on Alkyl Methyl Ammonium Chloride (ADBAC) in the Assay for Unscheduled DNA Synthesis in Rat Liver Primary Cell Cultures

AUTHOR: Marie E. McKeon

STUDY NUMBER: HWA #14778-0-447

DATE ISSUED: April 15, 1992

CONCLUSIONS: Negative for inducing unscheduled DNA synthesis (UDS) in primary rat hepatocytes (HPC) exposed *in vitro* up to cytotoxic doses (6.46 ug/ml).

TB-I EVALUATION: ACCEPTABLE

UDS Addendum

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

APR 15 1993

MEMORANDUM

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: ADBAC [Alkyl Dimethyl Benzyl Ammonium Chloride]--- Company Response and Data Submitted Under MRID # 422908-01 and 422908-02

ID # 069105

Chemical: 016-I (069105)
RD Record: S-425912
HED Project: D182923

FROM: Irving Mauer, Ph.D., Geneticist
Toxicology Branch-I
Health Effects Division (H7509C)
Irving Mauer 03-29-93

~~TO:~~ THRU: Brian Dementi, Ph.D., DABT
Review Section III
Toxicology Branch-I
Health Effects Division (H7509C)
Brian Dementi 4/13/93

~~FOR:~~ TO: Larry Schnaubelt/Brigid Lowry, PM #72
Reregistration Branch
Special Review and Reregistration Division (H7508W)

THRU: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch-I
Karl P. Baetcke 3/31/93

Registrant: ADBAC Quat Joint Venture (Huntington, Lonza, Mason, PPG, Sherex, and Stepan), submitted by the Chemical Specialties Manufacturers Association (CSMA), Washington, DC.

Request: Review and evaluate the following submissions from the registrant:

(1) Data from a mutagenicity assay, entitled:

Genotoxicity Test on Alkyl Dimethyl Ammonium Chloride (ADBAC) in the Assay for Unscheduled DNA Synthesis in Rat Liver Primary Cell Cultures, performed at Hazleton Washington, Inc. (HWA), Vienna, VA, HWA Project #14778-0-447, Final Report dated April 15, 1992. (EPA MRID #422908-01)

(2) Addendum (dated April 15, 1992) to a previously submitted mutagenicity study (MRID # 422908-02), entitled:

Mutagenicity Test on Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay, performed by Hazleton Labs. America (HLA), (HLA Study No. 10238-0-447), Report dated January 25, 1989 (EPA MRID No. 41012601), with Revision February 16, 1989,

which was judged UNACCEPTABLE for the following deficiencies: (DER attached to Memo: Mauer to Lee dated Oct. 13, 1989, HED Doc. # 007546):

(i) Repeat test required (to confirm initial negative).
(ii) Higher dose levels should be tested (up to demonstrable cytotoxicity).
(iii) The MP employed must be designated as the TGAI

(3) Another mutagenicity study, entitled:

Assessment of the Mutagenic Activity of Hyamine-3500 in the Mouse Micronucleus Test, performed by Scantox Biologisk Laboratorium A/S, Skensved (Denmark) for Lonza Inc., Fairlawn, NJ, Project #10753, Final Report dated December 16, 1985 (EPA MRID # 403111-01),

(4) Response to previous TOX-I review of the following mutagenicity study:

Mutagenicity Test on Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the CHO/HGPRT Foreward Mutation Assay, performed by Hazleton Labs., America (HLA), HLA Project # 10238-0-435, Final Report dated January 23, 1989 (EPA MRID # 41012701),

which was judged provisionally acceptable, pending receipt that the test article (designated 80% MP) was the formulation required by FIFRA regulations for generic testing (HED DOC #007546)

TB CONCLUSIONS:

ITEM (1): This genotoxicity (DNA damage/repair) assay (MRID #422908-01) is judged fully ACCEPTABLE in demonstrating negative results for UDS in primary rat hepatocyte cultures exposed up to cytotoxic concentrations, 6.46 ug/ml (see detailed review attached to this memo).

ITEM (2): The ADDENDUM (MRID #422908-02) provided acceptable supplemental information to the previously submitted Report judged UNACCEPTABLE, since

(i) Data from an adequate (ACCEPTABLE) repeat confirming the initial negative are available, as MRID 422908-01 (DER attached here).

(ii) Cytotoxicity was demonstrated at non-genotoxic higher dosages (10 to 11 ug/ml).

(iii) The test substance employed was a homogenous composite of commercial grade (MP) materials from the six manufacturers participating in the ADBAC Quat Reregistration Program, and this 80% manufacturing-use product has been accepted by the Agency for generic testing to generate toxicology (as well as environmental fate, and wildlife) data (LETTER: Lee to CSMA, dated June 24, 1987).

ITEM (3): The mouse micronucleus assay (MRID #403111-01) is judged Provisionally ACCEPTABLE in demonstrating negative cytogenetic results *in vivo* at a dose adversely affecting erythropoiesis (i.e. cytotoxic), pending submission of data from the preliminary dose-selection investigations, as well as characterization of the test article.

ITEM (4): The proviso for fully accepting the CHO/HGPRT mutagenicity assay is removed (as stated above) by the acceptance by the Agency of the 80% MP for generic (TGAI) testing for the generation of toxicology data (Lee to CSMA, dated June 24, 1987).

ATTACHMENT: DERs

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 11 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: ADBAC: Review of 2-Generation Reproduction Study (MRID 413850-01)

D167338
S400615
1-1953
Tox Chem No. 016E
PC Code 069105

FROM: Karen L. Hamernik, Ph.D.
Section Head, Section 3
Toxicology Branch I
Health Effects Division (H7509C) K.H 8/3/93

TO: Brigid Lowery, PM Team 72
Reregistration Branch
SRRD (H7508W)

THRU: Karl Baetcke, Ph.D.
Chief, Toxicology Branch I
Health Effects Division (H7509C)

Attached is the review of a two generation reproduction study in the Sprague-Dawley rat performed with Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) administered in the diet. The conclusions from the Data Evaluation Report are as follows:

Sprague-Dawley rats were administered 0, 300, 1000, or 2000 ppm of ADBAC daily in the diet over two generations. Clear evidence of toxicity was not observed even at the highest dose, although there were transient decreases in body weight gains and food consumption in F0 females at 2000 ppm. Consequently, the NOEL for parental toxicity was 2000 ppm (146 mg/kg/day male and female combined; 130.1 mg/kg/day, males and 160.9 mg/kg/day, females, averaged for the F0 and F1 generations). The LOEL for parental toxicity was not clearly established.

Reproductive toxicity seen at 2000 ppm (the LOEL) was evident as reduced pup body weights and body weight gain during lactation indicating an adverse effect on pup growth. Based on these results, the NOEL for developmental toxicity was 1000 ppm (73 mg/kg/day male and female combined; 65.4 mg/kg/day, males and 79.9 mg/kg/day, females, averaged for the F0 and F1 generations).

The study is considered to be Core Guideline for guideline 83-4.

EPA Reviewer: Ann Clevenger, Ph.D. Signature: [signature] for
Review Section I, Toxicology Branch I/HED Date: 8/23/93

EPA Section Head: Marion Copley, D.V.M. Signature: Marion Copley
Review Section IV, Toxicology Branch I/HED Date: 8/26/93

DATA EVALUATION REPORT

STUDY TYPE: Developmental toxicity in rats; Guideline Series 83-3

EPA IDENTIFICATION NUMBERS

PC CODE: 069105

TOX CHEM. NO.: 016 E

MRID NOS.: 423515-01 (Definitive study)
426451-01 (Range-finding study)

TEST MATERIAL: Alkyl Dimethyl Benzyl Ammonium Chloride

SYNONYM: ADBAC

SPONSOR: ADBAC QUAT Joint Venture/Chemical Specialties Manufacturers Association, Washington, DC

STUDY NUMBER: 91N0031

TESTING FACILITY: Bushy Run Research Center (BRRC), Export, PA

TITLE OF REPORT: Developmental Toxicity Evaluation II of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Administered by Gavage to CD® Rats

AUTHOR: T.L. Neeper-Bradley

REPORT ISSUED: June 8, 1992

CONCLUSIONS

Dose levels: 0, 10, 30, and 100 mg/kg/day

Administered by gavage on gestational days (GDs) 6-15, inclusively

NOEL (maternal) = 10 mg/kg/day
LOEL (maternal) = 30 mg/kg/day based on clinical signs (perioral wetness and audible respiration) and decreased body weight gain and food consumption

NOEL (developmental) = 100 mg/kg/day
LOEL (developmental) = not determined
> 100 mg/kg/d

FINAL

DATA EVALUATION REPORT

ALKYL DIMETHYL BENZYL AMMONIUM CHLORIDE

Study Type: Developmental Toxicity in Rabbits

Prepared for:

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by:

Clement International Corporation
9300 Lee Highway
Fairfax, VA 22031

Principal Reviewer:	Sanju Diwan Sanju Diwan, Ph.D.	Date	8/25/93
Independent Reviewer:	Pia Lindström Pia Lindström, D.P.H.	Date	8/25/93
QA/QC Manager:	Sharon A. Segal Sharon Segal, Ph.D.	Date	8/25/93

Contract Number: 68D10075
Work Assignment Number: 2-86, 2-121
Clement Number: 226
Project Officer: Caroline Cordon

EPA Reviewer: Ann Clevenger, Ph.D. Signature: 1/10 Hy
Review Section I, Toxicology Branch I/HED Date: 9/13/93

EPA Section Head: Marion Copley, D.V.M. Signature: Marion Copley
Review Section IV, Toxicology Branch I/HED Date: 9/8/93

DATA EVALUATION REPORT

STUDY TYPE: Developmental toxicity in rabbits; Guideline Series 83-3

EPA IDENTIFICATION NUMBERS

PC CODE: 069105

TOX CHEM. NO.: 016 E

MRID NO.: 423928-01 (Definitive study)
427344-01 (Range-finding study)

TEST MATERIAL: Alkyl dimethyl benzyl ammonium chloride

SYNONYM: ADBAC

SPONSOR: ADBAC QUAT Joint Venture/Chemical Specialties Manufacturers Association, Washington, DC

STUDY NUMBER: 91N0032

TESTING FACILITY: Bushy Run Research Center (BRRC), Export, PA

TITLE OF REPORT: Developmental Toxicity Evaluation of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) Administered by Gavage to New Zealand White Rabbits

AUTHORS: T.L. Neeper-Bradley and M.F. Kubena

REPORT ISSUED: July 8, 1992

CONCLUSIONS

Dose levels: 0, 1, 3, and 9 mg/kg/day

Administered by gavage on gestational days (GDs) 6-18, inclusively

NOEL (maternal) = 3 mg/kg/day
LOEL (maternal) = 9 mg/kg/day based on clinical signs (hypoactivity and labored and/or audible respiration)

NOEL (developmental) = 9 mg/kg/day
LOEL (developmental) = not determined > 9 mg/kg/d

WATER QUALITY GUIDELINE FOR THE PROTECTION OF FRESHWATER AQUATIC LIFE FOR DIDECYL DIMETHYL AMMONIUM CHLORIDE (DDAC)

FINAL COPY

Guidelines and Standards Division
Science Policy and Environmental Quality Branch
Environment Canada
Hull, Quebec

December 1998

Preface

Under the initiatives of the Fraser River Action Plan (FRAP), which includes the development of a co-operative management plan for sustainability of the Fraser River Basin, the restoration of fish and wildlife habitats, and the prevention of contamination of the basin's aquatic ecosystems and biota, national water quality guidelines for the protection of aquatic life are being developed to address concerns regarding the toxicity of antisapstains entering surface waters. Guideline derivation was undertaken by the Guidelines and Standards Division of Environment Canada which serves as the technical secretariat to the Canadian Council of Ministers of the Environment (CCME) Water Quality Task Group. The water quality guidelines will act as a management tool to assist in the protection of all forms and stages of aquatic life.

The role the Canadian Water Quality Guidelines plays is multifaceted, and includes;

- the assistance in protection and enhancement of aquatic and terrestrial resources;
- the assessment of environmental quality issues/concerns (*i.e.,* environmental yardsticks; early warning indicators);
- the establishment of site-specific environmental quality objectives;
- the provision of national targets for control and remediation programs; and
- the assessment of the efficacy of regulations.

The purpose of the Canadian Water Quality Guideline is not to provide a blanket value for national water quality. Due to the variations in environmental conditions across Canada, guidelines may need to be modified according to the local environment and/or socio-economic and technological factors. Site specific water quality objectives are established to reflect the local environment and concerns; these may be adopted into legislation to become standards for that jurisdiction.

Summary

A review of the environmental chemistry, fate, and toxicology of didecyl dimethyl ammonium chloride (DDAC) was conducted. DDAC is used in Canada in antisapstain formulations for treatment of freshly sawn lumber, in disinfectant formulations, and as a molluscicide. DDAC is an active ingredient in the most widely used antisapstain formulation (Kop-Coat NP-1), and one of the most widely used pesticides in British Columbia; 454 400 kg of DDAC were used by lumber mills for antisapstain purposes in 1996. DDAC, a cationic surfactant, is highly water soluble, and binds rapidly to suspended solids and sediments. It is not persistent in the water column; movement to the solid phase and microbial degradation are expected to be the main routes of dissipation. DDAC has been reported to affect rainbow trout *(Oncorhynchus mykiss)* at levels as low as 0.1 mg·L^{-1}, and *Daphnia magna* at levels as low as 0.03 mg·L^{-1}. It is not expected to bioaccumulate.

This review includes the development of the Canadian Water Quality Guideline for the Protection of Freshwater Aquatic Life for DDAC. An interim water quality guideline of 1.5 µg·L^{-1} is recommended which was derived according to the Canadian Council of Ministers of the Environment's (CCME) *Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life*, and is intended to be protective of all forms of freshwater aquatic life at all aquatic life stages.

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Glossary of Acronyms

BMP	Best Management Practices
CAS	Chemical Abstract Service
CCME	Canadian Council of Ministers of the Environment
CTAC	Cetyltrimethyl ammonium chloride
Cu-8	Copper-8-quinolinolate
CWQG	Canadian Water Quality Guideline
DDAB	Didecyl dimethyl ammonium bromide
DDAC	Didecyl dimethyl ammonium chloride
DO	Dissolved Oxygen
EC_{50}	Median Effective Concentration
FRAP	Fraser River Action Plan
GC	Gas chromatograph
IPBC	3-Iodo-2-Propynyl Butyl Carbamate
LC_{50}	Median Lethal Concentration
LOEC	Lowest Observable Effects Concentration
LOEL	Lowest Observable Effects Level
K_d	Partition Coefficient
K_{oc}	Organic-Carbon Sorption Partition Coefficient
K_{ow}	Octanol-Water Partition Coefficient
MATC	Maximum Acceptable Toxicant Concentration
NA	Not Applicable
NOEC	No Observable Effects Concentration
NOEL	No Observable Effects Level
QAC	Quaternary Ammonium Compound
TCMTB	2-(Thiocyanomethyl Thio) Benzothiazole
USEPA	Environmental Protection Agency
UV	Ultra-violet

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1 Introduction

Quaternary ammonium compounds (QAC) are a group of chemicals with powerful surfactant properties. Didecyl dimethyl ammonium chloride (DDAC) is a cationic QAC commonly used in disinfectant formulations. Recent applications of DDAC-containing formulations have been extended to include the treatment of freshly sawn lumber, and as a molluscicide to control zebra mussels.

The potential toxicity of DDAC to nontarget organisms in the aquatic environment arises from the addition of DDAC to inflow/outflow pipes to control zebra mussels, or accidental release from cooling towers utilising DDAC slimicide formulations, or other DDAC-containing formulations. In addition, the potential toxicity of antisapstain chemicals, including DDAC, is a concern as the mills typically using these chemicals occupy sites in close proximity to surface waters. Notwithstanding the efforts by the wood treatment industry to best manage and store freshly treated lumber in covered areas, during precipitation events, antisapstain chemicals may be leached or washed off of treated lumber stored in open areas, or from equipment used to move treated lumber. Thus, antisapstains may be released into the environment via storm water runoff.

Information regarding the environmental toxicology, chemistry, and fate of DDAC in the Canadian environment was gathered[1] from the open literature, unpublished data from academia and from industry (Lonza Inc.), and reviewed to assess the potential risk of aquatic contamination. This information was used to develop an interim Canadian Water Quality Guideline (CWQG) for the protection of freshwater life for DDAC. In addition, the development of CWQGs also requires data on current environmental contamination gathered by monitoring surveys. Guidelines developed in other jurisdictions are also considered. Information collected on the toxicology, fate, chemistry, and environmental concentrations of DDAC as well as the recommended CWQG for the protection of freshwater life are summarised here.

2 Production and Uses

DDAC (CAS registry number 7173-51-5) is a quaternary ammonium compound (QAC), a group of chemicals commonly used as industrial disinfectants, and is registered in Canada for use as a molluscicide (full registration), in formulated disinfectants (full registration), recirculating cooling towers (full registration), and as an antisapstain (temporary registration). It is an active ingredient in commercial antisapstain aqueous formulations[2], molluscicide formulations, slimicide formulations and industrial disinfectant formulations[3].

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[1] See Appendix I for databases searched.
[2] Refer to Appendix II for antisapstain products and active ingredient concentrations.
[3] Refer to Appendix III for products and active ingredient concentrations.

3 Physical and Chemical Properties

DDAC is a non-volatile, photolytically stable QAC with a molecular weight of 361.5 g·mol^{-1}, a chemical formula of $C_{22}H_{48}NCl$ (see Figure 1), and is produced as a water soluble salt in an aqueous solution at 80 % active ingredient. It has low vapour pressure (Solomon 1990) and is highly water soluble (Agriculture Canada *et al.* 1989); the solubility calculated to be 700 mg·L^{-1} (Boethling and Lynch 1992) (see Table 1). The log octanol/water coefficient (log K_{ow}) is estimated to be 0; DDAC is equally soluble in both water and octanol, producing a ratio K_{ow} of 1, and a log K_{ow} of 0 (Nixon 1998). DDAC does not hydrolyse in water (ABC Laboratories Inc. 1989b), suggesting negligible chemical degradation in the water column.

Soil adsorption tests have indicated that DDAC has a high capacity for soil adsorption and is essentially immobile in soil. Reported log soil adsorption coefficient (K_{oc}) values range from 5.64 (sand) to 6.20 (silty clay loam; ABC Laboratories Inc. 1989a). The cationic properties of DDAC likely allows for strong binding with anionic sites in soils and sediments.

Because DDAC is not produced as a pure substance, physical and chemical properties of commercial DDAC mixtures were also located. DDAC production initially yields a product termed a manufacturer's use product, and may be 50 or 80% DDAC. The pH of 80% DDAC "manufacturer's use product " (*i.e.*, Bardac 2280) at room temperature is 7.81, and is a colourless liquid free from visible foreign matter at 20°C with a density of 0.870 g·mL^{-1} and a flashpoint of 29.5°C. Pure DDAC has been produced, but only at a laboratory scale. This was done by purifying Bardac 2280 by recrystalisation using benzene to remove ethanol and drying techniques to remove water (Bestari *et al.* 1997).

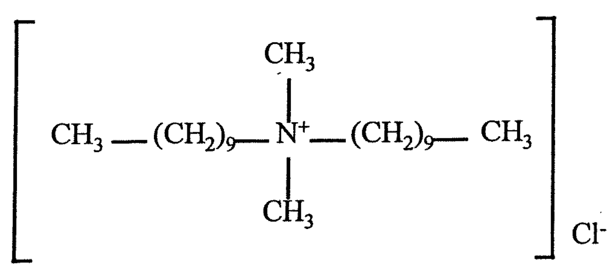

Figure 1 The chemical structure of DDAC.

Colourimetric methods are also used to determine levels of DDAC in aqueous samples. DDAC is complexed with disulphine blue in chloroform; the concentration of the complex is then measured using UV spectrophotometry. Detection limits may vary using this method, but are estimated at 50 $\mu g \cdot L^{-1}$ (Schoenig, G.P., pers. comm. 1998).

DDAC concentrations in wood preservative formulations have been determined by using a Parr oxygen bomb for combustion of the sample to convert all chlorine present to the ionic form (Koppers Company Inc. 1984). Total chlorine can then be determined using titration methods. DDAC concentrations in the range of 2-10% total chlorine can be determined with the use of this method.

5 Mode of Action

The mode of action of DDAC has not been systematically studied in any aquatic organism and remains unknown. Because DDAC is a surfactant, a mode of action can be attributed to binding to cell surface causing cell membrane disruption and protein denaturation, leading to cell death. The end result is tissue damage of those areas directly exposed to DDAC. This is most likely to occur at high concentrations; however, whether or not such tissue damage effects cause the lethality observed with routine toxicity test is unknown. Wood *et al.* (1996a), for example, found no external disruptions to fish gill lamellae using scanning electron microscopy. This contrasts the situation with TCMTB for which severe lamellar epithelial disruption is reported (Nikl and Farrell 1993). The acute toxicity curve of DDAC is very steep, suggesting an all-or-none type of lethal toxicity; the range of mortality is typically much less than an order of magnitude (Farrell *et al.* 1998a) and in various fish and invertebrates, the NOEC was within 50% of the LC_{50} value (summarized in Henderson 1992).

TRS (1997) has suggested that in aquatic organisms (*e.g.,* fish and invertebrates), DDAC acts primarily via the gill epithelia and acts to hinder gas transfer to the point of suffocation. Observed sub-lethal effects include head shaking and laboured respiration (TRS 1997). This, however, has been neither confirmed nor refuted using respiratory techniques. The observed sub-lethal effects of head shaking and laboured respiration are typical of most fish that are dying regardless of the toxicant and its mode of action.

The sublethal effects of short-term exposures were studied in rainbow trout and starry flounder (Farrell *et al.* 1998a; Wood *et al.* 1996a). DDAC exposure caused an increase in both trout and flounder lactate but not in their haematocrit, leucocrit, or haemoglobin.

In terrestrial organisms, DDAC damages the gut epithelia reducing water and nutrient uptake. Effects in rats and dogs were observed as decreases in body weight and food consumption, as well as severe dehydration resulting from gastrointestinal effects (Bushy Run Research Centre 1988; Hazleton Washington Inc. 1991).

IPBC and DDAC as Kop-Coat NP-1. The top 2-3 cm were collected from the Eckmann dredge that was used; the outer 2 cm rim of the sample contacting the dredge was discarded. DDAC concentrations ranged from 0.57 to 1.26 $\mu g \cdot g^{-1}$ dry weight. The percent moisture for these samples ranged from 44 to 62% (Szenasy 1998).

6.4 Biota

No information was found on the environmental concentrations of DDAC in biota. Bioaccumulation is discussed further in Section 7.4.

6.5 Atmospheric Transport

No information was found on the environmental concentrations of DDAC in the atmosphere. DDAC has low potential for atmospheric contamination, as it is a non-volatile compound. It may, however, escape to the atmosphere via antisapstain formulation spraying, although transport of the droplets, of DDAC adhered to particles, has not been investigated.

7 Environmental Fate and Persistence

When considering the environmental fate and persistence of DDAC, two key physico-chemical properties are important; one is the lipophilic alkyl moiety, the other is the cationic moiety, which, because of its association with chloride, allows the molecule to be hydrophilic.

DDAC is stable to many of the processes typically influencing the environmental fate of a compound or chemical. Microbial degradation and adsorption, however, can significantly affect its fate and persistence. Because the release of DDAC into the environment is tied to precipitation events, the frequency and severity of rainfall events, and receiving water volume and flow rate (*i.e.*, during freshet) may also affect the environmental fate of DDAC (Szenasy and Bailey 1996).

DDAC generally degrades first by the alkyl chain. This should be taken into consideration with respect to those studies which use a radiolabel on the N-methyl group of the molecule.

7.1 Water and Sediment

The fate of DDAC is largely dependent on the nature of the receiving waters. Additionally, the suspended solids content, and microbial population in the water and sediment, and/or the composition of the sediment matrix underlying the receiving water may affect degradation. This is especially important in the case of cationic surfactants like DDAC, which readily adsorbs to most surfaces, including those of sediment and suspended solids.

this may be explained by the heterogeneous nature of most sediment samples, with regard to both matrix composition and microbial population.
QACs have been demonstrated to bind as strongly to sediment as sewage (Boethling 1984) which allows comparison with studies studying QAC degradation in sewage treatment. Using shaker flask methods, DDAC added to a mixed microbial inoculum of three loam soil samples, an activated sewage sludge sample and a raw influent sewage sample is ultimately degraded; 80.92% of the theoretical CO_2 being evolved, and 84.46% of the dissolved organic carbon being removed after 28 days (ABC Laboratories Inc. 1993). It should be noted that this study included a 14-day acclimation of the microbial inoculum to DDAC prior to testing. Acclimation may allow for an increased rate of DDAC biodegradation (Boethling 1984).

In summary, the microbial degradation of DDAC may be dependent on the nature of the receiving waters. The composition of the sediment will largely dictate the rate and degree of removal of DDAC from the water column. In the same way, the microbial population will affect the rate of degradation; very little degradation can be expected in sediment where there is no microbial population.

7.1.2 Hydrolysis and Volatilisation

DDAC has been reported to be non-volatile (Agriculture Canada *et al.* 1989), and stable to hydrolysis (ABC Laboratories Inc. 1989b). ^{14}C-DDAC (labelled on the N-methyl group) showed no evidence of degradation at 10 mg·L^{-1} after 30 days in a sterile, dark environment at 25°C and pH 5, 7 and 9 (ABC Laboratories Inc. 1989b).

7.1.3 Photodegradation

ABC Laboratories Inc. (1989c) reported that DDAC is stable to the effects of photolysis. No degradation of ^{14}C-DDAC (labelled on the N-methyl group) was detected after 30 days at 25°C, pH 7, and constant xenon arc light exposure. Only 7% degradation occurred in the presence of the photosensitizer acetone after 30 d under the same conditions, the half-life for which was calculated to be 227 days.

7.2 Soils

DDAC in soil is largely resistant to factors commonly associated with the degradation of other compounds or chemicals in soil such as volatilisation, photodegradation and hydrolysis. Strong adsorption and limited degradation potential suggest that DDAC contamination in soil may persist at high concentrations.

7.2.1 Microbial Degradation

DDAC was found to be stable in soil, with a half-life of 1048 days in microbially active sandy loam spiked with 10 mg·kg^{-1} ^{14}C-DDAC, maintained at 25°C for one year. At the end of the study, 72.9% of radioactivity was found in the parent compound and

One study examined the bioconcentration and elimination of DDAC and its residues by bluegill sunfish, *Lepomis macrochirus* (Springborn Laboratories Inc. 1990e) exposed to an average measured concentration of 93 $\mu g \cdot L^{-1}$ DDAC. Following the onset of exposure, the concentration of ^{14}C residues (DDAC, degradation products and metabolites) reached a steady state in 10 days. The mean steady state bioconcentration factor for the 28 day exposure was 38 for edible portions (muscle/skin), 140 for inedible portions (viscera/carcass), and 81 for whole body tissues. ^{14}C residue levels sorbed to the skin and scales was 2-6 times that of the edible tissue portion, indicating significant binding to the skin and scales. An 18 day depuration period followed the exposure period. 67% of the ^{14}C residues had been eliminated by day 14 of the depuration period.

8 Toxicology

All of the available toxicological studies relating to DDAC were ranked, according to the Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life (CCME 1991), as primary, secondary, or unacceptable. In the following discussion, emphasis will be placed on the primary and secondary studies; studies ranked unacceptable are noted as such.

8.1 Fish

8.1.1 Freshwater

Acute Toxicity

The range of toxicity of DDAC to fish is represented by a broad range of data (see Figure 2, Table 2). The available data from ten species reported values ranging from a 24-h lowest observable effects level (LOEL) of 0.1 mg a.i.$\cdot L^{-1}$ for the swimming performance of rainbow trout, *Oncorhynchus mykiss* (Wood *et al.* 1996a) to a 96-h median lethal concentration (LC_{50}) of 1.05 mg Bardac 2280$\cdot L^{-1}$ for coho salmon (*Oncorhynchus kisutch*; Farrell *et al.* 1998a).

The 96-h LC_{50} for bluegill sunfish *(Lepomis macrochirus)* exposed to Bardac 2280 during a static test was 0.32 mg a.i.$\cdot L^{-1}$ (Springborn 1990a). Channel catfish (*Ictalurus punctatus*; 0.8-1.2 g) were exposed to Calgon H-130 in a static test for 48 h yielding a LC_{50} of 0.71 mg a.i.$\cdot L^{-1}$ (Waller *et al.* 1993).

Farrell *et al.* (1998a) exposed various life stages of coho salmon *(Oncorhynchus kisutch)* to Bardac 2280 using a 96-h static renewal system. The 96-h LC_{50} for embryos were 0.583 mg Bardac 2280$\cdot L^{-1}$ at 0-4 d, and 1.05 mg Bardac 2280$\cdot L^{-1}$ at 42-46 d. Alevins were more sensitive than the embryos; 96-h LC_{50} were reported as 0.423 mg Bardac 2280$\cdot L^{-1}$ at 67-71 d, 0.385 mg Bardac 2280$\cdot L^{-1}$ at 76-80 d, 0.456 mg Bardac 2280$\cdot L^{-1}$ at 86-90 d, and 0.489 mg Bardac 2280$\cdot L^{-1}$ at 104-108 d. Coho salmon smolt sensitivity was less than that of the alevin and fry, with an LC_{50} of 0.948 mg Bardac 2280$\cdot L^{-1}$. Another system. The toxicity of DDAC to sturgeon fry decreased 15-fold with addition of Fraser River sediment from a 96-h LC_{50} of 0.416 to 6.50 mg a.i.$\cdot L^{-1}$ (Aqua-Science 1997). Toxicity to fathead minnow fry decreased five-fold with the addition of Fraser River sediment from a 96-h LC_{50} of 0.19 to 1.0-3.0 mg a.i.$\cdot L^{-1}$, or with the use of Fraser River water (96-h LC_{50} = 1.0-3.0 mg a.i.$\cdot L^{-1}$); the no observable effects concentration (NOEC) for fathead minnow in a seven day test decreased more than 13-fold, from 0.19 to 2.5 mg a.i.$\cdot L^{-1}$ (TRS 1997). These studies suggest that DDAC bioavailability to aquatic organisms is reduced following binding to either suspended solids or sediment, as may occur in a natural river system.

Chronic Toxicity

Limited information on the chronic toxicity of DDAC to fish was found (see Figure 2, Table 2). The range of concentrations where lethality increases from 0% to 100% is very narrow, and chronic effects within this range are not likely to be seen. The mode of action for chronic effects, however, may act via a mechanism unrelated to acute toxicity. Although, currently, this remains largely unknown.

Fathead minnow larvae were exposed to Calgon H-130 in a seven day static renewal test. The lowest observable effects concentration (LOEC) and maximum acceptable toxicant concentration (MATC) were reported to be 0.75 and 0.53 mg a.i.$\cdot L^{-1}$, respectively. These endpoints are for both mortality and growth observation (Resource Analysts Inc. 1990). This was the only study found to investigate chronic DDAC toxicity.

8.1.2 Marine

The available data from two species of fish: Springborn Laboratories Inc. (1994a) reported a 96-h LC_{50} of 0.940 mg a.i.$\cdot L^{-1}$ for the sheepshead minnow *(Cyprinodon variegatus)*, and Farrell et al. (1998a) reported a 96-h LC_{50} of 2.05 mg Bardac 2280$\cdot L^{-1}$ for the starry flounder *(Platichthys stellatus)* (see Table 3).

8.2 Amphibians and Reptiles

No information was found on the toxicity of DDAC to amphibians or reptiles.

8.3 Invertebrates

8.3.1 Freshwater

Reported DDAC toxicity data for nine species of invertebrates ranged from a 48-h LC_{50} of 0.037 mg Bardac 2280$\cdot L^{-1}$ for *Daphnia magna* (Farrell *et al.* 1998a) to a 48-h LC_{50} of 6.12 mg a.i.$\cdot L^{-1}$ for the threehorn wartyback mussel, *Obliquaria reflexa* (Waller *et al.* 1993) (Figure 2, Table 4).

tripling or one third and so on. An index of 5.1 therefore indicates a six-fold increase in toxicity due to the interaction of DDAC and IPBC. Because Kop-Coat NP-1 is used so widely in coastal British Columbia mills, this additivity to some species may have deleterious environmental effects.

Experiments have been conducted to compare the toxicity of DDAC in laboratory water and in site water, or with laboratory water with site sediment added. The NOEC for *D. magna* in a seven day test increased 10-fold, from 0.038 - 0.38 mg a.i.$\cdot$L^{-1} (TRS 1997). This study demonstrates the amelioration of aquatic DDAC toxicity in the presence of sediment.

8.3.2 Freshwater Sediments

The toxicity of DDAC to sediment-dwelling organisms was investigated using *H. azteca* and a clean sediment sample from the upper Fraser Basin (77.1% sand 16.3% silt, 6.4% clay), spiked with DDAC. The study reported a 14-d LC_{50}, LOEL, and NOEL of 1099.8, 1000, and 750 µg a.i.$\cdot$g^{-1}; respectively. There were no observed effects of DDAC on the growth of *H. azteca* (Szenasy 1998). *Chironomus tentans* were also exposed to DDAC-spiked sediment in a 28-d chronic study, where a LC_{50} of 2085 µg$\cdot$g^{-1}, and a chronic LOEC (emergence) of 1000 µg a.i.$\cdot$g^{-1} were reported (TRS 1997).

In addition to the *H. azteca* study, Szenasy (1998) also investigated the toxicity of DDAC-spiked sediment using solid phase Microtox®. Concentrations of 1500 µg a.i.$\cdot$g^{-1} and greater were found to be toxic to the bacteria; concentrations of 1000 µg a.i.$\cdot$g^{-1} and less were non-toxic to the bacteria.

Concurrent to the 14-d *H. azteca* testing, the toxicity of the water overlying DDAC-spiked sediment to *D. magna* was determined. A LC_{50} of 2250 µg a.i.$\cdot$g^{-1} was determined, as was a LOEL of 3000 µg a.i.$\cdot$g^{-1}, and a NOEL of 1500 µg a.i.$\cdot$g^{-1}. These values correspond to concentrations in the water of 1033 µg a.i.$\cdot$L^{-1}, 1609.5 µg a.i.$\cdot$L^{-1}, and 456 µg a.i.$\cdot$L^{-1}, respectively. In addition, all mortalities occurred in the first 48 h, and all observations resulted in either 0 of 100% mortality. There were no observed effect on reproduction (Szenasy 1998). These observations are comparable to the amelioration studies performed with site water and *Ceriodaphnia dubia* (TRS 1997). The static nature of laboratory experiments, however, may reduce bioavailability compared with natural system; the water flow of natural systems would keep sediments in suspension, which may act to increase bioavailiblity as smaller particles would come in more intimate contact with body surfaces, in particular, gas exchange surfaces.

product, Bardac 2280. Due to the expense of conducting studies using the active ingredient alone all of the data collected were based on the formulated product; Bardac 2280, which contains 80% active ingredients. Therefore, it is appropriate that, in this particular circumstance, the guideline for the active ingredient (DDAC) be set using toxicity data for the formulated product (Bardac 2280). This was taken into account when calculating the DDAC concentration eliciting toxicity.

10.2 Marine Life

Insufficient data was located to derive a water quality guideline for the protection of marine life according to the protocol (CCME 1991).

11 Data Gaps

The data gaps identified in the following discussion prevent complete understanding of the fate and persistence of DDAC in the Canadian environment, and the toxicity of DDAC to aquatic organisms. While sufficient data were collected to derive interim guidelines, fulfilling the data gaps will allow for the derivation of full guidelines for the protection of freshwater biota.

11.1 Chemical and Physical Properties, and Environmental Fate and Persistence

For a full guideline, further data on the fate and persistence of DDAC in the environment, and the related chemical and physical properties are required. Current evidence suggests that DDAC is removed from the water column primarily by sorbing onto sediments and suspended solids, and not by hydrolysis, volatilisation, or photodegradation. Adsorption of DDAC by the sediment will reduce toxicity to aquatic organisms. Biotransformation would likely occur subsequently, as suggested by the fate of other QACs in sediment. Therefore, information on the fate and toxicity of DDAC bound to suspended solids and receiving water sediments (as opposed to sewage or sludge sediments) is necessary. In addition, further research is needed that would clarify the bioavailability and persistence of DDAC in sediment, which in turn, may contribute to the development of a Canadian sediment quality guideline for DDAC.

11.2 Toxicology

There is a general data gap with respect to the mode of action of DDAC. There is also little information available regarding the chronic toxicity of DDAC which is of vital importance for the derivation of a full guideline.

In order to develop a full guideline, the following additional studies are required. Two primary chronic fish studies on at least two species resident in North America other than rainbow trout; one must be a warm-water species. Two primary chronic invertebrate studies on at least two species resident in North America but from different classes are

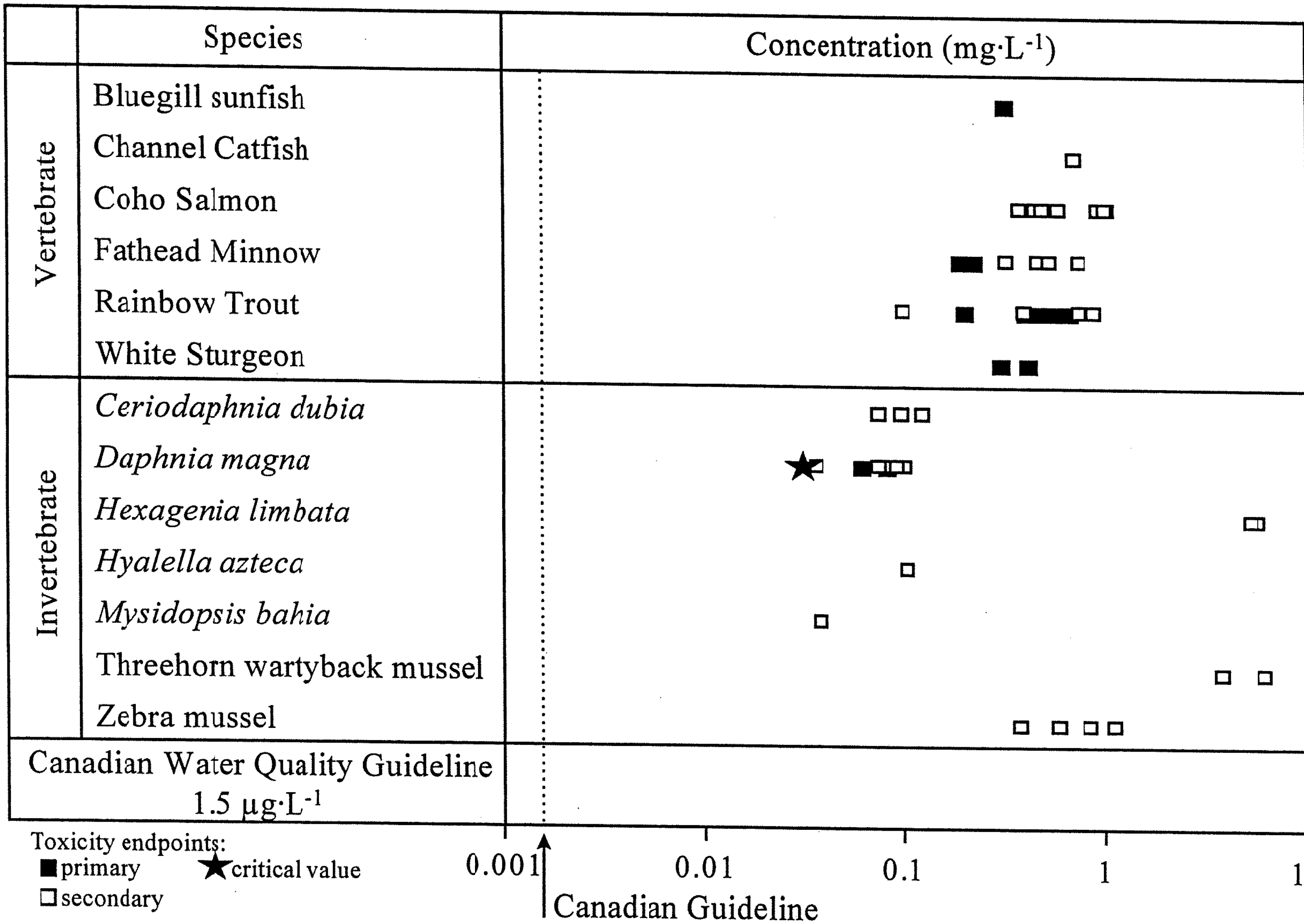

Figure 2 Toxicity of DDAC to freshwater organisms.

Table 2 Acute and Chronic Toxicity of DDAC to Freshwater Fish

Test Organism	Life Stage	Test Type	Dur. (h)	Effect (mg a.i.·L^{-1})[a]	Temp (°C)	DO (mg·L^{-1})[a]	pH	Hardness (mg·L^{-1} $CaCO_3$)	Formulation	Data Type	Reference
Bluegill sunfish *(Lepomis macrochirus)*	NR	S, U	48	LC_{50} = 0.38	NR	NR	NR	NR	Bardac 22	UN	Kruger and Vogin 1971
Bluegill sunfish	NR	S, U	96	LC_{50} = 0.3	NR	NR	NR	NR	Bardac 22	UN	Kruger and Vogin 1971
Bluegill sunfish	NR	NR	24	LC_{50} = 0.60	NR	NR	NR	NR	Bardac 22	UN	Wells Laboratories Inc. 1971a
Bluegill sunfish	NR	NR	48	LC_{50} = 0.30	NR	NR	NR	NR	Bardac 22	UN	Wells Laboratories Inc. 1971a
Bluegill sunfish	NR	NR	96	LC_{50} = 0.27	NR	NR	NR	NR	Bardac 22	UN	Liu 1990a
Bluegill sunfish	26-47 mm 0.24-0.85 g	S, M	96	LC_{50} = 0.32 NOEC = 0.1	22-25	> 60 % saturation	8.0	50	Bardac 22	1	Springborn Laboratories Inc. 1990a
Catfish (species NR)	NR	S, U	48	LC_{50} = 2.4	NR	NR	NR	NR	Bardac 22	UN	Kruger and Vogin 1971
Catfish (species NR)	NR	S, U	96	LC_{50} = 1.3	NR	NR	NR	NR	Bardac 22	UN	Kruger and Vogin 1971
Channel catfish *(Ictalurus punctatus)*	0.8-1.2 g	S, U	48	LC_{50} = 0.71	17	> 60 % saturation	7.7	40	Calgon H-130	2	Waller *et al.* 1993
Chinook salmon *(Oncorhynchus tshawytscha)*	NR	S, U	96	LC_{50} = 0.36	NR	NR	NR	NR	F-2	UN	Walker Brothers undated
Chinook salmon	NR	FT, U	96	LC_{50} = 0.77-0.80[b]	NR	NR	NR	NR	Kop-Coat NP-1	UN	Environment Canada 1987
Coho salmon *(Oncorhynchus kisutch)*	E, 0-4 d	SR, U	96	LC_{50} = 0.583[b]	8	NR	6.1-6.7	6.0	Bardac 2280	2	Farrell *et al.* 1998a
Coho salmon	E, 42-46 d	SR, U	96	LC_{50} = 1.050[b]	8	NR	6.1-6.7	6.0	Bardac 2280	2	Farrell *et al.* 1998a
Coho salmon	AL, 67-71 d	SR, U	96	LC_{50} = 0.423[b]	10	NR	6.1-6.7	6.0	Bardac 2280	2	Farrell *et al.* 1998a
Coho salmon	AL, 76-80 d	SR, U	96	LC_{50} = 0.385[b]	10	NR	6.1-6.7	6.0	Bardac 2280	2	Farrell *et al.* 1998a
Coho salmon	AL, 86-90 d	SR, U	96	LC_{50} = 0.456[b]	10	NR	6.1-6.7	6.0	Bardac 2280	2	Farrell *et al.* 1998a
Coho salmon	F, 104-108 d	SR, U	96	LC_{50} = 0.489[b]	12	NR	6.1-6.7	6.0	Bardac 2280	2	Farrell *et al.* 1998a
Coho salmon	SM	SR, U	96	LC_{50} = 0.948[b]	12	NR	6.1-6.7	6.0	Bardac 2280	2	Farrell *et al.* 1998a
Coho salmon	35-52 mm 0.24-1.14 g	S, M	96	LC_{50} = 1.0 NOEC = 0.59	11-13	> 60 % saturation	7.6	38	Bardac 22	1	Springborn Laboratories Inc. 1990b
Coho salmon	12-16 d	FT, U	96	LC_{50} = 0.485[b] LOEL = 0.420[b] NOEL = 0.320[b]	12	NR	6.2-6.8	5.2-6.0	8 parts Bardac 2280 1.03 parts P-100	UN	Farrell *et al.* 1998b
Coho salmon	6-7 mo.	FT, U	96	LC_{50} = 0.424[b] LOEL = 0.420[b] NOEL = 0.320[b]	12	NR	6.2-6.8	5.2-6.0	8 parts Bardac 2280 1.03 parts	UN	Farrell *et al.* 1998b

Table 2 Acute and Chronic Toxicity of DDAC to Freshwater Fish

Test Organism	Life Stage	Test Type	Dur. (h)	Effect (mg a.i.·L^{-1})[a]	Temp (°C)	DO (mg·L^{-1})[a]	pH	Hardness (mg·L^{-1} $CaCO_3$)	Formulation	Data Type	Reference
Coho salmon	NR	S, U	96	LC_{50} = 0.67	NR	NR	NR	NR	P-100 F-2	UN	Environment Canada 1990a
Fathead minnow (*Pimephales promelas*)	35-47 mm 0.39-0.91 g	S, M	96	LC_{50} = 0.19	22-24	> 60 % saturation	7.1-7.3	40-42	Bardac 2280	1	Springborn Laboratories Inc. 1994a
Fathead minnow	J	SR, U	96	LC_{50} = 0.328	25	NR	6.1-6.7	6.0	Bardac 2280	2	Farrell *et al.* 1998a
Fathead minnow	L, < 24h	SR, U	24	LC_{50} = 0.47[b]	24.8-25.1	8.0-8.2	8.0-8.2	NR	Calgon H-130	2	Bargar 1991
Fathead minnow	J	FT, M	96	LC_{50} = 0.195 LOEC = 0.224 NOEC = 0.122	22	> 60 % saturation	8.2-8.4	128	Bardac 2280	1	Wildlife International Ltd. 1995b
Fathead minnow	< 24 h	SR, U	7d	LOEC = 0.75[b] NOEC = 0.38[b] MATC = 0.53[b]	25	5.8-8.6	6.4-8	50-92	Calgon H-130	2	Resource Analysts Inc. 1990
Guppy (*Poecilia reticulata)*	NR	NR	48	LC_{50} = 0.95	NR	NR	NR	NR	Bardac 22	UN	Centraal Laboratorium TNO 1978
Guppy	NR	NR	96	LC_{50} = 0.6	NR	NR	NR	NR	Bardac 22	UN	Centraal Laboratorium TNO 1978
Rainbow trout (*Oncorhynchus mykiss)*	J, 1+ y	FT, U	96	LC_{50} = 0.41[b]	12	NR	6.1-6.7	6.0	Bardac 2280	2	Farrell *et al.* 1998a
Rainbow trout	NR	NR	24	LC_{50} = 0.63	NR	NR	NR	NR	Bardac 22	UN	Frances 1971
Rainbow trout	NR	NR	48	LC_{50} = 0.59	NR	NR	NR	NR	Bardac 22	UN	Frances 1971
Rainbow trout	NR	S, U	96	LC_{50} = 2.48	NR	NR	NR	NR	Timbercote II	UN	Liu 1990b
Rainbow trout	NR	S, U	96	LC_{50} = 0.44	NR	NR	NR	NR	F-2	UN	Liu 1990b
Rainbow trout	NR	NR	96	LC_{50} = 2.81	NR	NR	NR	NR	NR	UN	Liu 1990b
Rainbow trout	NR	NR	96	LC_{50} = 0.55	NR	NR	NR	NR	Bardac 22	UN	Wells Laboratories Inc. 1971b
Rainbow trout	NR	S, U	96	LC_{50} = 0.52	NR	NR	NR	NR	F-2	UN	Environment Canada 1990b
Rainbow trout	J	FT, M	96	LC_{50} = 0.466 LOEC = 0.53 NOEC = 0.38	12	> 60 % saturation	8.2-8.5	136	Bardac 2280	1	Wildlife International Ltd. 1995c
Rainbow trout	J	S, M	96	LC_{50} = 0.66 LOEC = 0.43 NOEC = 0.26	12	> 60 % saturation	7.9-8.5	132	Bardac 2280	1	Wildlife International Ltd. 1995d
Rainbow trout	NR	NR	96	LC_{50} = 1.24	NR	NR	NR	NR	NR	UN	Agriculture Canada *et al.* 1989
Rainbow trout	NR	FT, U	96	LC_{50} = 0.49-0.94[b]	NR	NR	NR	NR	Kop-Coat NP-1	UN	Environment Canada 1987
Rainbow trout	J, 8.67 g	FT, U	12	NOEL = 0.1 LOEL = 0.2 (swimming)	12	> 95 % saturation	6.8-6.9	5.2-6.0	Bardac 2280	2[c]	Wood *et al.* 1996a
Rainbow trout	J, 8.67 g	FT, U	48	NOEL = 0.2 LOEL = 0.4 (swimming)	12	> 95 % saturation	6.8-6.9	5.2-6.0	Bardac 2280	1[c]	Wood *et al.* 1996a
Rainbow trout	J, 8.67 g	FT, U	96	LC_{50} =0.409	12	> 95 %	6.8-6.9	5.2-6.2	Bardac 2280	1[c]	Wood *et al.* 1996a

Table 2 Acute and Chronic Toxicity of DDAC to Freshwater Fish

Test Organism	Life Stage	Test Type	Dur. (h)	Effect (mg a.i.·L^{-1})[a]	Temp (°C)	DO (mg·L^{-1})[a]	pH	Hardness (mg·L^{-1} $CaCO_3$)	Formulation	Data Type	Reference
Rainbow trout	0.8-1.2 g	S, U	48	LC_{50} = 0.75	17	saturation > 60 % saturation	7.7	40	Calgon H-130	2	Waller *et al.* 1993
Rainbow trout	0.6 g	S, U	96	LC_{50} = 0.88 [b]	15	10	6.1-6.7	NR	Bardac 2280	2	Environment Canada 1989
Rainbow trout	J, 8.67 g	FT, U	24	NOEL = 0.4 (HIS, liver glycogen, leucocrit, haemoglobin, haematocrit) NOEL = 0.2 LOEL = 0.4 (glucose, lactate, cortisol) LOEL = 0.1 (swimming)	12	> 95 % saturation	6.8-6.9	5.2-6.0	Bardac 2280	2[c]	Wood *et al.* 1996a
Rainbow trout	J	FT, U	96	LC_{50} = 0.457 [b] LOEL = 0.420 [b] NOEL = 0.320 [b]	13	NR	6.2-6.8	5.2-6.0	8 parts Bardac 2280 1.03 parts P-100	UN	Farrell *et al.* 1998b
White sturgeon (*Acipenser transmontanus)*	F, 78d	SR, UN	96	LC_{50} = 0.416 LC_{25} = 0.225 LOEC = 0.300 NOEC = 0.100	16-17	8.5-9.7	7.05-7.74	94-135	Bardac 2280	2	ETS 1997a
White sturgeon	L, < 1 w	S, UN	24	LC_{50} = 0.00074	15	> 6.0	6.5-7.5	< 34.1	Bardac 2280	U[d]	Bennett 1996; Bennett and Farrell 1998
White sturgeon	F, 42d	S, UN	24	LC_{50} = 0.001-0.01	15	> 6.0	6.1-6.7	< 34.1	Bardac 2280	U[d]	Bennett 1996; Bennett and Farrell 1998
White sturgeon	F, 104d	SR, UN	96	10 g·L^{-1} Fraser R. sediment LC_{50} = 5.22 LC_{25} = 3.814 LOEC = 8.03 NOEC = 2.409	17	3.3-9.6	6.52-8.85	43-119	Bardac 2280	U	ETS 1997b

Note: Dur. = duration; Temp. = temperature; DO = dissolved oxygen; A = adult; J = juvenile; SM = smolt; F = fry; AL = alevin; L = larvae; E = embryo; S = static; SR = static renewal; FT = flow through; U = unmeasured concentration; M = measured concentration; 1 = primary; 2 = secondary; NR = not reported; UN = unacceptable

[a] unless otherwise noted
[b] mg formulation ·L^{-1}
[c] nominal concentrations, but DDAC is very stable and subsequent analyses yielded measured concentrations 81.5 % of the nominal concentrations
[d] unacceptable for the purposes of guidelines derivation

Table 3 Acute Toxicity of DDAC to Marine Fish

Test Organism	Life Stage	Test Type	Dur. (h)	Effect (mg a.i. ·L^{-1})[a]	Temp (°C)	DO (mg·L^{-1})[a]	pH	Hardness (mg·L^{-1} $CaCO_3$)	Formulation	Data Type	Reference
Sheepshead minnow (*Cyprinodon variegatus*)	22-35 mm 0.19-0.39 g	S, M	96	LC_{50} = 0.940 NOEL = 0.390 (32 ‰ salinity)	21-22	3.2-7.4	7.7-8.1	NR	Bardac 2280	UN	Springborn Laboratories Inc. 1994b
Starry flounder (*Platichthys stellatus*)	J, 1+ y	FT, U	96	LC_{50} = 2.05[b] (15 ‰ salinity)	12	NR	6.1-6.7	6.0	Bardac 2280	UN	Farrell *et al.* 1998a

Note: Dur. = duration; Temp. = temperature; DO = dissolved oxygen; A = adult; J = juvenile; SM = smolt; F = fry; AL = alevin; L = larvae; E = embryo; S = static; SR = static renewal; FT = flow through; U = unmeasured concentration; M = measured concentration; 1 = primary; 2 = secondary; NR = not reported; UN = unacceptable

[a] unless otherwise noted
[b] mg formulation ·L^{-1}

Table 4 Acute and Chronic Toxicity of DDAC to Freshwater Invertebrates

Test Organism	Life Stage	Test Type	Dur. (h)[a]	Effect (mg a.i. ·L^{-1})[a]	Temp (°C)	DO (mg·L^{-1})[a]	pH	Hardness (mg·L^{-1} $CaCO_3$)	Formulation	Data Type	Reference
Ceriodaphnia dubia	NE	SR,U	7 d	100% mortality at lowest conc. (0.5 mg·L^{-1} with 2.5 mg·L^{-1} bentonite clay)[b]	23.7-24.8	6.6-7.9	7.8-8.0	NR	Calgon H-130	UN	Bargar 1991
C. dubia	NE	S, U	24	LC_{50} = 0.076[b]	24.8-25.1	7.9-8.2	7.7-8.0	NR	Calgon H-130	2	Bargar 1991
C. dubia	< 24 h	SR, U	7d	LOEC = 0.125[b] NOEC = 0.075[b] MATC = 0.097[b] (mortality and reproductive success)	25	7.8-9.3	7.4-7.8	33-63	Calgon H-130	2	Resource Analysts Inc. 1990
Daphnia magna	NE	S, U	48	LC_{50} = 0.102[b] LOEL = 0.089[b] NOEL = 0.067[b]	22	NR	7.5	180	Bardac 2280	2	Farrell *et al.* 1998a
D. magna	NE	SR, U	96	LC_{50} = 0.093[b] LOEL = 0.075[b] NOEL = 0.050[b]	20	NR	7.5	80-100	Bardac 2280	2	Farrell *et al.* 1998a
D. magna	L	SR, U	21 d	NOEL = 0.037[b] (fecundity)	22	NR	8.1-8.3	180	Bardac 2280	2	Farrell *et al.* 1998a
D. magna	NE	SR, U	48	LC_{50} = 0.037[b]	20	NR	8.1-8.3	180	Bardac 2280	2	Farrell *et al.* 1998a
D. magna	NR	S	48	LC_{50} = 0.094 NOEC = 0.074 (no endpoint specified)	NR	NR	NR	NR	Bardac 22	UN	Springborn Laboratories Inc. 1990c
D. magna	< 24 h	FT, M	48	EC_{50} = 0.062 LOEC = 0.081 NOEC = 0.048	18-22	> 60 % saturation	8.2-8.4	132	Bardac 2280	1	Wildlife International Ltd. 1995a
D. magna	< 24 h	SR, U	48	LC_{50} = 0.105[b] LOEL = 0.75[b]	23	NR	7.9-8.2	180	8 parts Bardac 2280 1.03 parts P-100	UN	Farrell *et al.* 1998b
D. magna	< 24 h	S, U	48	LC_{50} = 0.037[b] LC_{50} = 0.030[bc]	22	NR	7.53	80-100	Bardac 2280	2	Farrell *et al.* 1998a
Hexagenia limbata	NY, 12-33 mm	S, U	24	LC_{50} = 5.7[b] EC_{50} = 5.2[b] (movement when prodded)	19	7.8-8.1	7.2-7.9	NR	Calgon H-130	2	Bargar 1991
H. limbata	NY, 12-33 mm	S, U	48	no significant mortality at highest concentration (100 with 500 bentonite	19	7.5-8.1	7.9-8.3	NR	Calgon H-130 (50 %)	UN	Bargar 1991

Table 4 Acute and Chronic Toxicity of DDAC to Freshwater Invertebrates

Test Organism	Life Stage	Test Type	Dur. (h)[a]	Effect (mg a.i. $\cdot L^{-1}$)[a]	Temp (°C)	DO ($mg \cdot L^{-1}$)[a]	pH	Hardness ($mg \cdot L^{-1}$ $CaCO_3$)	Formulation	Data Type	Reference
				clay)[b]							
Hyalella azteca	2-9 d	SR, U	48	LC_{50} = 0.026[b] LOEL = 0.019[b] NOEL = 0.014[b]	25	NR	7.9-8.2	180	8 parts Bardac 2280 1.03 parts P-100	UN	Farrell *et al.* 1998b
H. azteca	NR	SR, U	96	LC_{50} = 0.106[b]	25	NR	8.1-8.3	180	Bardac 2280	2	Farrell *et al.* 1998a
Mysidopsis bahia	< 7 d	SR, U	96	LC_{50} = 0.039[b]	25	NR	8.1-8.3	180	Bardac 2280	2	Farrell *et al.* 1998a
Threehorn wartyback mussel (*Obliquaria reflexa*)	A, 30-50 mm	S	48	LC_{50} = 6.12 LC_{50} (post exposure) = 3.72	17	> 60 % saturation	7.7	40	Calgon H-130	2	Waller *et al.* 1993
Zebra mussel (*Dreissena polymorpha*)	A, 5-8 mm	S, U	48	LC_{50} = 0.85 LC_{50} (post exposure) = 0.38	17	> 60 % saturation	7.7	40	Calgon H-130	2	Waller *et al.* 1993
Zebra mussel	A, 20-25 mm	S,U	48	LC_{50} = 1.12 LC_{50} (post exposure) = 0.59	17	> 60 % saturation	7.7	40	Calgon H-130	2	Waller *et al.* 1993

Note: Dur. = duration; Temp. = temperature; DO = dissolved oxygen; A = adult; NE = neonate; NY= nymph; L = lifecycle; S = static; SR = static renewal; FT = flow through; U = unmeasured concentration; M = measured concentration; 1 = primary; 2 = secondary; NR = not reported; UN = unacceptable

[a] unless otherwise noted
[b] mg formulation $\cdot L^{-1}$
[c] LC_{50} recalculated from raw data (Farrell *et al.* 1998a) using a four parameter logistic model (α<0) (Caux and Moore 1997) by Environment Canada

Table 5 Acute Toxicity of DDAC to Marine Invertebrates

Test Organism	Life Stage	Test Type	Dur. (h)[a]	Effect ($mg \cdot L^{-1}$)	Temp (°C)	DO ($mg \cdot L^{-1}$)	pH	Hardness ($mg \cdot L^{-1}$ $CaCO_3$)	Formulation	Data Type	Reference
Eastern oyster (*Crassostrea virginica*)	29-49 mm valve height	S, M	96	EC_{50} = 0.13 NOEC = 0.072 (32 ‰ salinity)	21-22	4.7-6.7	7.1-7.9	NR	Bardac 2280	UN	Springborn Laboratories Inc. 1994c
Mysidopsis bahia	< 24 h	S, M	96	LC_{50} = 0.069 NOEL = 0.052 (32 ‰ salinity)	23-24	5.6-7.6	8.0-8.2	NR	Bardac 2280	UN	Springborn Laboratories Inc. 1990d

Note: Dur. = duration; Temp. = temperature; DO = dissolved oxygen; A = adult; NE = neonate; NY= nymph; L = lifecycle; S = static; SR = static renewal; FT = flow through; U = unmeasured concentration; M = measured concentration; 1 = primary; 2 = secondary; NR = not reported; UN = unacceptable

Table 6. Acute Toxicity of DDAC to Freshwater Plants

Test Organism	Life Stage	Test Type	Dur. (d)	Effect ($mg \cdot L^{-1}$)	Temp (°C)	DO ($mg \cdot L^{-1}$)	pH	Hardness ($mg \cdot L^{-1}$ $CaCO_3$)	Formulation	Data Type	Reference
Duck weed (*Spirodella oligorhiza*)	NR	S, U	3	growth suppressed following 3 d exposure to 10^{-5} M [a]	25	NR	NR	NR	Bardac 22	UN	Walker and Evans 1978
Green alga (*Chlorella sp.*)	NR	S, U	3	growth suppressed following 3 d exposure to 10^{-5} M [a]	25	NR	NR	NR	Bardac 22	UN	Walker and Evans 1978

Note: Dur. = duration; Temp. = temperature; DO = dissolved oxygen; Form. = formulation; S = static; SR = static renewal; FT = flow through; U = unmeasured concentration; M = measured concentration; 1 = primary; 2 = secondary; NR = not reported; UN = unacceptable

[a] mg formulation $\cdot L^{-1}$

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Wildlife International Ltd. 1996. Aerobic aquatic biodegradation test with didecyldimethylammoniumchloride (DDAC) and a bentonite clay: DDAC complex conducted with natural sediment and site water. Submitted to Lonza Inc., Fairlawn, NJ. 78 pp.

Wildlife International Ltd. 1997. Product chemistry testing of Bardac 2280. Submitted to Lonza Inc., Fairlawn, NJ. 70 pp.

Appendix I Databases Used for Bibliographic Search

Aqualine
AQUIRE (Aquatic Toxicity Information Retrieval Database)
ASFA (Aquatic Sciences and Fisheries Abstracts)
ASTER (Assessment Tools for the Evaluation of Risk)
BIOSIS (Dialog)
CAB Abstracts (Dialog)
Canadian Research Index
CCINFO
CESARS (Chemical Evaluation Search and Retrieval System)
Chemical Abstracts
Current Contents
ELIAS (Environmental Library Integrated Automated System)
Enviroline (Dialog)
Environmental Bibliographies (Dialog)
Environmental Abstracts
EPAOLS (Environmental Protection Agency On-Line Services)
GeoRef (Dialog)
HSDB (Hazardous Substance DataBase)
Life Sciences Collection (Dialog)
NTIS (Dialog)
Pascal (Dialog)
Pollution Abstracts (Dialog)
RTECS
SCI (Scientific Citation Index)
Toxline (Dialog)
UNCOVER
Water Resources Abstracts (Dialog)

Appendix II Formulated antisapstain products containing DDAC.

Registration	Product Name	Guar.	STAR
23947	BARDAC 2250 R QUAT CONCENTRATED LIQUID GERMICIDE	50.0	R
23946	BARDAC 2280 R QUAT CONCENTRATED LIQUID GERMICIDE	80.0	R
25106	BTC 1010-80% CONCENTRATED GERMICIDE	80.0	R
21760	ECOBRITE III SAPSTAIN CONTROL PRODUCT	2	H
21939	F2 CONCENTRATE T2154 LIQUID MICROBICIDE	11.4	R
21753	KOP-COAT NP-1 SAPSTAIN CONTROL CHEMICAL	64.56	R
20321	LONZA BARDAC 2280	80	R
24812	MAQUAT 4450-E	50	R
24805	MAQUAT 4480-E	80	R
24058	QC-2 SAPSTAIN CONTROL PRODUCT	28.0	R
24059	QC-3 SAPSTAIN CONTROL PRODUCT	28.0	R
21982	TIMBERCOTE 2000 SAPSTAIN CONTROL PRODUCT	28.O	R
21773	TIMBERCOTE II (SAPSTAIN CONTROL PRODUCT)	20	H

Guar. = Guarantee in %
STAR = Status of Registration (R=Registered, H=Historical)

Appendix III Formulated products containing DDAC

Registration	Product Name	Guar.	STAR
17468	3-D ULTRA-4 CONCENTRATE ALL-PURPOSE CLEANER	1.26	R
23652	3M QUAT DISINFECTANT CLEANER CONCENTRATE	3.906	R
24041	3M SANITIZER CONCENTRATE	2.31	R
24555	AB-787 DISINFECTANT	1.350	R
23814	ACQ-2B COMPONENT FOR WOOD PRESERVATIVE ACQ	80	R
23092	ACTERGE DISINFECTANT CLEANER	1.650	R
17756	ACTION DSC LIQUID CLEANER DISINFECTANT	4.5	R
24480	AF79 CONCENTRATE DISINFECTANT CLEANER	0.684	R
15206	AG-411 INDUSTRIAL LIQUID MICROBIOCIDE	20	R
21976	AGRO-SQUAD 2+ DISINFECTANT CLEANER	3.906	R
21974	AGRO-SQUAD 2-I DISINFECTANT CLEANER	1.953	R
24222	ALLSTAR CARPET CSD (CARPET SANITIZING CONCENTRATE)	0.36	R
24287	ALLSTAR DC DISINFECTANT/CLEANER	0.684	R
19921	ANTISTAF DISINFECTANT CLEANER	0.57	R
20842	A-QUAT DISINFECTANT	1.05	R
22041	AVALON PHONE WIPE	0.007 4	R
22049	AVALON TOILET WIPE	0.007 4	H
23907	BAC-A-TAC DISINFECTANT CLEANER	1.953	R
24219	BACSTOP FABRIC SANITIZER	50	R
24668	BACTERGE DISINFECTANT CLEANER	1.953	R
21723	BARDAC 205 M	9.0	R
21899	BARDAC 2050	15.0	R
18208	BARDAC 205M-7.5 DISINFECTANT SANITIZER	1.125	R
21726	BARDAC 208 M	14.4	R
21897	BARDAC 2080 (TECHNICAL)	24.0	R
17466	BARDAC 2210 DISINFECTANT SANITIZER	7.5	R
21893	BARDAC 2250 MANUFACTURING CONCENTRATE	50	R
23947	BARDAC 2250 R QUAT CONCENTRATED LIQUID GERMICIDE	50.0	R
23946	BARDAC 2280 R QUAT CONCENTRATED LIQUID GERMICIDE	80.0	R
21055	BASIC-G HIGHLY CONCENTRATED GERMICIDAL SOLUTION	1.875	R
24481	BETCO 256 DISINFECTANT CLEANER	2.250	R
20370	BIOGUARD 453 DISINFECTANT CLEANER	0.662	R
20367	BIOGUARD 903 DISINFECTANT CLEANER	1.628	R

Registration	Product Name	Guar.	STAR
20082	ENDBAC 256 DISINFECTANT CLEANER	3.255	R
24487	ENDBAC 256 DISINFECTANT CLEANER	8.70	R
24701	ENDBAC 256 SUPER CONC. DISINFECTANT CLEANER	8.70	R
23612	ENDEW FABRIC MILDEW INHIBITOR & SANITIZER	50	R
24740	ENVIRO SOLUTIONS 64 GENERAL PURPOSE NEUTRAL DISINFECTANT	3.857	R
24720	ENVIRO-SOLUTIONS 256 NEUTRAL DISINFECTANT CONCENTRATE	15.36	R
18633	ENZ-ALL DISINFECTANT CLEANER	0.990	R
20843	EPQUAT DISINFECTANT SANITIZER	2.250	R
23639	EQUALITY HOUSEHOLD CLEANER & DISINFECTANT (PINE SCENT)	0.324	R
22057	ESTEAM SANI-CLEAN DISINFECTANT CLEANER	0.456	R
23964	EXO DISINFECTANT CLEANER	3.906	R
23854	EXTRA KLEEN DISINFECTANT CLEANER	1.953	R
20689	F-11 DISINFECTANT	1.125	R
21939	F2 CONCENTRATE T2154 LIQUID MICROBICIDE	11.4	R
22729	FINALE GERMICIDAL DETERGENT	0.152	R
24044	FMB 1210-5 QUAT CONCENTRATED LIQUID GERMICIDE	30.0	R
24043	FMB 1210-8 QUAT CONCENTRATED LIQUID GERMICIDE	48.0	R
20712	FORMULA 3473 INDUSTRIAL LIQUID MICROBICIDE	5	R
17791	FORMULA D375 LIQUID CLEANER DISINFECTANT	2.5	H
24883	FORMULATION HWS-128 GERMICIDAL DETERGENT & DEODORANT	4.61	R
24890	FORMULATION HWS-256	9.22	R
24879	FORMULATION HWS-64	1.54	R
22440	FORMULATION S-23-15	0.72	H
22441	FORMULATION S-39	0.324	H
22273	FORMULE Q-75 DISINFECTANT	1.350	H
23207	FULLTROL PLUS 128 CLEANER DISINFECTANT	1.953	R
23442	FUL-TROLE DISINFECTANT CLEANER	0.324	R
20222	G-10 DISINFECTANT-SANITIZER-FUNGICIDE-DEODORIZER	3.00	R
23156	G-1085 DISINFECTANT CLEANER	1.953	R
19736	G-700 DISINFECTANT-CLEANER-SANITIZER	1.26	R
22816	GERM FREE	0.990	R
23416	GERMICIDAL DETERGENT	0.540	R
23198	GERMITOL 128 CLEANER DISINFECTANT	1.953	H
21320	GERM-O-SOLV 2 CLEANER DISINFECTANT	4.5	R
19095	GLIDERINSE III DISINFECTANT SANITIZER FUNGICIDE	1.125	R
22836	H-130 MICROBIOCIDE	50	R

Registration	Product Name	Guar.	STAR
	CLEANER		
23268	LONZA FORMULATION S-18F	1.953	R
18451	LONZA FORMULATION S-21-7 DISINFECTANT CLEANER	0.990	R
23272	LONZA FORMULATION S-21F	0.990	R
17467	LONZA FORMULATION S-37-3 DISINFECTANT-CLEANER	1.26	R
23261	LONZA FORMULATION S-37F	1.26	R
19898	LONZA FORMULATION S-38-3 DISINFECTANT CLEANER	0.684	R
23265	LONZA FORMULATION S-38F	0.684	R
22439	LONZA FORMULATION Y-59-125	0.461	H
17770	LONZA WATER TREATMENT MICROBIOCIDE	50	R
25248	LYSOL BRAND DISINFECTANT DEODORIZING CLEANER	0.075	R
23807	LYSOL BRAND FOAMING DISINFECTANT BASIN TUB & TILE CLEANER	0.05	R
23808	LYSOL BRAND FOAMING DISINFECTANT BASIN TUB & TILE CLEANER	0.05	R
22739	MAGNA CAS-5 DISINFECTANT SANITIZER	2.250	R
22973	MAGNA Q-25 DISINFECTANT CLEANER	3.750	R
22720	MAGNA Q-43 DISINFECTANT CLEANER	6.510	R
20275	MAGNACIDE 509 INDUSTRIAL BACTERICIDE	12.5	R
22613	MAGNATROL 443-A LIQUID MICROBIOCIDE	50	R
19427	MAGNICIDE 785 INDUSTRIAL BACTERICIDE	20	R
25410	MAQUAT 40-50		R
25407	MAQUAT 40-80		R
24812	MAQUAT 4450-E	50	R
24805	MAQUAT 4480-E	80	R
25408	MAQUAT MQ615M	7.5	R
25409	MAQUAT MQ624M	12.0	R
24928	MCD LIQUID SANITIZER	0.684	R
23568	MEDI-QUAT 4 DISINFECTANT CLEANER	1.953	R
24666	MEGA QUAT DISINFECTANT CLEANER	3.906	R
20339	MILDIQUAT 50 LIQUID LAUNDRY MILDEW INHIBITOR	50	R
23147	MIROQUAT DISINFECTANT	0.990	R
22176	NCP GENERAL PURPOSE DISINFECTANT	0.660	H
22648	ND-700 DISINFECTANT CLEANER	0.84	H
24904	NUTRA QUAT DISINFECTANT CLEANER SANITIZER	7.68	R
23495	OASIS 499 DISINFECTANT CLEANER	6.510	R
22058	OMNIQUAD 666 DISINFECTANT CLEANER	1.5	R
24547	OPTI-MAX DG-100	1.953	H
13148	PACE CHEMICALS CHEMPROCIDE DISINFECTANT	7.5	R

Registration	Product Name	Guar.	STAR
17501	SANEX AIRTROL SANICIDE	4.5	R
24524	SANEX CARPET SANITIZING CONCENTRATE	0.36	R
20296	SANFAX GENI-SEP DISINFECTANT CLEANER	3.255	H
23083	SANI CLEAN DISINFECTANT CLEANER	2.10	R
20221	SANIMASTER III DISINFECTANT CLEANER	1.05 (OR 1.049)	H
20344	SANI-QUAT DISINFECTANT CLEANER	4.5	R
23146	SANITAR DISINFECTANT	7.5	R
23140	SANITOR DISINFECTANT	1.350	R
23573	SANITROL MB DISINFECTANT CLEANER	1.350	R
17774	SAVOLITE QUATRASOL LIQUID CLEANER DEODORIZER	1.875	R
22230	SHAKLEE BASIC GERMICIDE (HIGHLY CONCENTRATED)	2.25	H
18346	SLUYTER DISINFECTANT CLEANER	4.5	R
18233	SPARTAN CHEMICALS GERMICIDAL LIQUID DETERGENT	1.44	R
21856	SPECIALNET CLEANER-DISINFECTANT	0.99	R
23155	SPUR-TEX 829 QUATERNARY SANITIZER (DISINFECTANT)	1.35	H
23108	STATE FORMULA 640 TERG-O-CIDE	0.684	R
22789	SUMA QUAT HIGH DILUTION QUATERNARY GERMICIDAL CLEANER	2.250	R
19102	SUPER BACTACIDE DISINFECTANT CLEANER	1.05	R
20726	SUPER STEROL #1 DISINFECTANT-CLEANER	0.825	R
20725	SUPER STEROL #2 DISINFECTANT-CLEANER	0.57	R
20295	SUPERSTAR DISINFECTANT CLEANER	0.57	H
24667	SURE 5 DISINFECTANT CLEANER	0.990	R
22542	SWEEN SURE-CIDE PLUS DISINFECTANT LIQUID CLEANER	2.250	R
19960	SYNET CLEANER DISINFECTANT	0.234	R
24749	T-350 WATER TREATMENT MICROBIOCIDE	50.0	R
23014	THREE STAR DEODORIZING CLEANER DISINFECTANT	0.324	R
23017	THREE STAR DEODORIZING CLEANER DISINFECTANT PINE SCENT	0.324	R
21982	TIMBERCOTE 2000 SAPSTAIN CONTROL PRODUCT	28.O	R
21773	TIMBERCOTE II (SAPSTAIN CONTROL PRODUCT)	20	H
17771	TRETOLITE X-CIDE 507 INDUSTRIAL LIQUID MICROBIOCIDE	50	R
24161	TRIAD II DISINFECTANT CLEANER	1.14	R

Appendix IV Bioassay Summary for Critical Study (Farrell *et al.* 1998a, pers. com.)

Test Substance: didecyldimethylammonium chloride (DDAC)
Product Information: Bardac 2280® (80% DDAC, 10% ethanol, 10% water)
Lonza Inc., Fairlawn, N.J.
Source of Test Organism: Aquatic Research Organisms, New Hampshire
Test Species: *Daphnia magna* (< 24 h old)
Water Supply: U.S. EPA Moderately Hard Synthetic

Date	1994	15/06-30/07/94	7/09-28/09/94	16/10/96
Temperature (°C ± 1°C)	22	20	20	22
Test Water Volume (mL)	40	25	25	50
Hardness ($mg \cdot L^{-1}$ $CaCO_3$)	80-100	80-100	80-100	180
Salinity (‰)	0	0	0	0
pH	7.53	7.53	7.53	7.5
Nominal Test Conditions $\mu g \cdot L^{-1}$ Bardac 2280® ($\mu g \cdot L^{-1}$ DDAC)	0 (0) 10 (8) 22 (17.6) 46 (36.8) 100 (80) 222 (176)	0 (0) 20 (16) 30 (24) 50 (40) 75 (60) 100 (80) 125 (100) 150 (120)	0 (0) 15 (12) 30 (24) 50 (40) 75 (60) 100 (80) 125 (100)	0 (0) 67 (54) 89 (71) 116 (93) 142 (114) 178 (142) 231 (185)
NOEL $\mu g \cdot L^{-1}$ Bardac 2280® ($\mu g \cdot L^{-1}$ DDAC)	-	50 (40)	30 (24)	67 (54)
LOEL $\mu g \cdot L^{-1}$ Bardac 2280® ($\mu g \cdot L^{-1}$ DDAC)	22 (17.6)	75 (60)	50 (40)	89 (71)
EC_{100} $\mu g \cdot L^{-1}$ Bardac 2280® ($\mu g \cdot L^{-1}$ DDAC)	100 (80)	125 (100)	125 (100)	142 (114)
LC_{50} $\mu g \cdot L^{-1}$ Bardac 2280® ($\mu g \cdot L^{-1}$ DDAC)	37 (30)	93.0 (74.4)	73.6 (58.8)	102 (82)
LC_{50} 95% Confidence Interval $\mu g \cdot L^{-1}$ Bardac 2280® ($\mu g \cdot L^{-1}$ DDAC)	28-48 (22-38)	80.7-103.7 (64.6-82.9)	60.0-88.3 (48.0-70.6)	91-114 (73-91)
Statistical Analysis Method	Probit	Probit	Probit, ANOVA	Probit

BC Environment

A REVIEW OF THE ENVIRONMENTAL IMPACT AND TOXIC EFFECTS OF DDAC

N.D. Henderson
Prepared for:
Environmental Protection Division
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SUMMARY

This paper summarizes the physical, chemical, environmental, and toxicological properties of didecyldimethylammonium chloride (DDAC), an active ingredient in several antisapstain products used by the Canadian lumber industry.

Laboratory studies have shown that DDAC is photolytically and hydrolytically stable, and immobile in soil. These studies also show that DDAC is resistant to microbial degradation, although earlier study results showed complete degradation within 48 hours when DDAC was incorporated into mixed bacterial soil and sewage cultures. Differences in studies and findings suggest that the composition of the microbial population is an important variable in the degradation of DDAC. The concentration of DDAC also appears to be an important variable since in another laboratory study, high primary degradation was found at a DDAC level of 5 ppm while poor ultimate degradation was observed at 15 ppm. Predicted half-lives in the soil and aquatic environments are 3 years, and 17 to 23 years, respectively. These half-lives are calculated from studies of much shorter duration (i.e. 30 days, one year) than the calculated half-lives.

In two leaching studies using DDAC treated lumber, DDAC concentrations between 48 and 73.2 ppm were found in the initial leachates. The concentrations of DDAC in later leachates in both studies were in the 6 ppm range.

In rats, DDAC is minimally absorbed from the gastrointestinal tract. It is excreted in the urine and feces, and a negligible amount is retained in the body after one week. It is moderately to very toxic to mammals orally and dermally, depending on formulation and according to toxicity scales used in this report. It is a severe eye and skin irritant.

Using toxicity scales derived for this paper and others, DDAC is slightly to very toxic to salmonid species, depending on formulation. DDAC is also extremely toxic to mysid shrimp, and is highly phytotoxic to an alga and a duckweed. In a bluegill bioconcentration study, DDAC was found to reach steady-state levels rapidly in fish tissue and to depurate rapidly (7 to 14 day half-life) following re-exposure to untreated water. The bioconcentration factor in edible fish tissue was determined to be 38x, suggesting little likelihood for bioaccumulation in fish tissue.

DDAC has displayed no carcinogenic, mutagenic, or teratogenic activity in laboratory tests. The observed severe irritation effects observed in laboratory animals suggests that acute human exposure may result in severe effects through skin and eye contact, or through ingestion. The use of DDAC in the workplace should not pose a significant health risk provided proper protective equipment is worn and proper safety practices are observed.

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1.0 INTRODUCTION

Large volumes of chlorophenol compounds have previously been used in Canada to preserve and protect wood from attack by various pests. Concerns about acute aquatic toxicity, occupational impacts, and presence of hazardous impurities, including dioxins and furans, in chlorophenols are among the reasons for dissatisfaction with their use (5). The Canadian lumber industry has thus phased out the use of chlorinated phenols for sapstain control, and the use of alternative chemicals has increased.

Currently there are several chemicals registered with Agriculture Canada which may be used for the protection of freshly cut lumber, including 3-iodo-2-propynyl butyl carbamate (IPBC), didecyldimethylammonium chloride (DDAC), sodium carbonate, sodium borate, azaconazole, and copper-8-quinolinolate (Cu-8).

The purpose of this paper is to review and evaluate available information concerning the physical and chemical properties, environmental behaviour, and toxicological effects of DDAC. This chemical is an active ingredient in a number of antisapstain formulations, including NP-1, Timbercote II, F-2, and Ecobrite III. Information on NP-1 is included in a separate report (39), while information on the other formulations is included where available. Information on non-formulated DDAC is also included. Companies marketing products containing the chemical were contacted for information, and a literature search of selected computerized databases was carried out (Appendix A).

2.0 HISTORICAL BACKGROUND AND USES

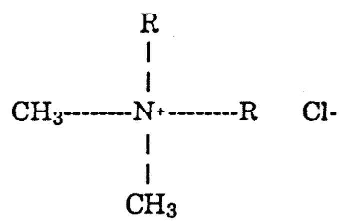
DDAC is a quaternary ammonium compound (QAC), and is a member of a group of such chemicals well known for their germicidal, fungicidal, and algicidal activity. QACs were first synthesized in the late 1800's, and their bactericidal properties were reported about two decades later. By 1935, their germicidal and antiseptic potential had been characterized. Since that time, extensive research on toxicity and side effects has been carried out. Presently, formulations containing between 0.01 and 1.0% QACs are used as antiseptics, bactericides, fungicides, sanitizers, and deodorants (21). QACs are also popular disinfectants for utensils, containers, and other instruments used in restaurants, dairies, food plants, laundries, and operating rooms (21).

DDAC formulations have long been used as antimicrobials and antiseptics in hospital and industrial settings (1). Bardac 2280, 80% DDAC in an alcohol/water base, is one such product. Manufactured by Lonza Inc., it has found

found wide use as a disinfectant, sanitizer, household cleaner, mildew preventative in commercial laundries, and microbicide in water treatment (7). DDAC is currently registered in Canada as an anti-microbial, and as an active ingredient in the antisapstain products NP-1, F-2, Timbercote II, and Ecobrite III (66). Appendix B lists registered products containing DDAC, and their manufacturers.

3.0 PHYSICAL AND CHEMICAL PROPERTIES

The chemical structure of DDAC is shown below.



(R = C_{10})

(CAS No. 7173-51-5)

DDAC is a nonvolatile, photolytically stable salt which is highly soluble in water (2). Its octanol/water partition coefficient is reportedly zero (2, 64), so bioconcentration and bioaccumulation are not expected to occur. Data on other physical properties such as boiling point, freezing point, and density were not located. Bardac 2250, manufactured by Lonza Inc., contains 50% DDAC, 9-11% ethanol, 32.8-40% water, and 2-5% other minor constituents. It has a flash point of 42°C, a specific gravity of 0.927 at 25°C, and a pH of 6.5 to 9.0. It is soluble in water, ethanol, and glycols, and is dispersible in hydrocarbons. Bardac 2280 contains 80% DDAC, 9-11% ethanol, 1.8-8.55% water, and the remainder other minor constituents (70). Its flashpoint is 43°C, and its specific gravity is 0.891 at 25°C. The pH and solubility characteristics are similar to Bardac 2250 (79).

Timbercote II is composed of 20% DDAC, 2.5% ethyl alcohol, and a synthetic resin in aqueous emulsion (40). It has a boiling point of 100°C, a freezing point of 0°C (30), a pH of 5 to 7, and a specific gravity of 0.989 (40). It has poor freeze/thaw stability and its vapour pressure is unknown (69). The resin component is a vinyl acetate copolymer emulsion with a pH of 4 to 6 and a specific gravity of 1.05-1.15. It is a non-flammable white fluid with a mild acetic acid odour. Hazardous decomposition products of this copolymer emulsion include carbon monoxide, carbon dioxide, and possibly traces of vinyl acetate (30).

F-2, composed of 11.4% DDAC and 16.8% borax, is a translucent amber liquid emulsion with a mild detergent odour. It has a pH between 7 and 8, a specific gravity of 1.077, and a flashpoint greater than 90°C. It is stable at 25°C, and has some freeze-thaw stability (64). F-2 is 100% soluble in water at 20°C, and is insoluble in oil.

Because NP-1 contains another active ingredient in addition to DDAC, the physical and chemical characteristics of NP-1 are included in another review (39). Information on Ecobrite III was not available.

One source states that incineration of DDAC is regarded as safe (22), although temperature and other details of incineration were not stated. Another source states that potentially toxic fumes may form and include carbon dioxide, carbon monoxide, ammonia, nitrogen oxides, and hydrogen chloride gas (2). Dioxins reportedly do not form (49). Further details on incineration of DDAC were not available.

4.0 ENVIRONMENTAL IMPACT

4.1 Environmental Sources

DDAC is not known to be naturally occurring, so all DDAC in the environment is expected to be from human sources. Such sources could include spills and other unpermitted discharges, permitted discharges from commercial facilities using the chemical, and discharges from products treated with DDAC, including wood, laundered items, and sterilized equipment and utensils.

4.2 Environmental Distribution

No studies on levels of DDAC in ambient air, water, or soil were located.

4.3 Environmental Behaviour

Several laboratory-based environmental fate studies, including aerobic soil metabolism, and aerobic and anaerobic aquatic metabolism studies, have been completed and submitted by the manufacturer. These studies are summarized below. Field studies on the environmental fate of DDAC are also being planned by the manufacturer, such that the behaviour of the compound in real environments (as opposed to laboratory environments) may be better understood. These studies should be completed in 1992 (99).

4.3.1 Photolysis

A study conducted with carbon-14 labelled DDAC at 25°C in aqueous buffered solution (pH 7) found the chemical to be stable to photolysis (12). A xenon light source, simulating natural sunlight, continuously illuminated the solution for 30 days. At the end of this time, no significant degradation of the test compound had occurred. In the presence of the photosensitizer acetone, approximately 7% of the parent compound was degraded. The photolysis rate constant and half life for this system were calculated to be 0.00304/day and 227 days, respectively. An accurate measure of the photolytic half life could not be determined since no significant degradation occurred.

4.3.2 Hydrolysis

A 30 day hydrolysis study using carbon-14 labelled DDAC at 25°C in aqueous solutions buffered to pH 5, 7, and 9 found the chemical to be stable within this pH range (13). All experiments were conducted at a nominal test concentration of 10 ug/ml, under sterile conditions and in darkness. An accurate measure of the hydrolytic half life could not be determined since no significant degradation occurred.

4.3.3 Soil/Sediment Adsorption/Desorption

A soil adsorption/desorption study conducted at 25°C in the dark with four soil types found that the chemical was immobile in all soils tested (14). The study was conducted at a 1:200 soil to water ratio using four nominal concentrations of 0.70, 3.50, 5.25, and 7.00 ppm DDAC in sand, sandy loam, silty clay loam, and silt loam (0.25, 0.90, 2.05, and 2.1% organic carbon, respectively). The study concluded that DDAC is essentially immobile in soil. Consequently, DDAC in soil would be unlikely to contaminate groundwater.

4.3.4 Biotransformation and Soil Metabolism

Biotransformation is expected to be the main route of dissipation of DDAC in the environment (2). An older, completed study indicated that rapid and complete degradation of DDAC occurs within 48 hours when low concentrations (10 ppm) are exposed to mixed bacterial cultures obtained from soil and sewage (34). A laboratory examination of the biodegradability of DDAC found a high primary degradation at a level of 5 ppm, but a poor ultimate degradation at 15 ppm (65).

In contrast to the above studies, a one-ye aerobic soil metabolism study recently submitted by the manufacturer found t t DDAC is stable to microbial degradation (93). The study used a microbially active sandy loam treated at a nominal concentration of 10 ppm of ^{14}C-DDAC, and incubated in the dark at 25°C. Soil samples collected at 0, 1, 3, 7, 14, 31, 61, 92, 123, 182, 273, and 365 days after dosing were extracted and analyzed for ^{14}C-DDAC. Following the incubation period, 72.9% of the dosed radioactivity remained as parent compound. An aerobic half-life of 1,048 days (~3 years) was calculated, based on first-order degradation. However, an accurate measure of the soil half life could not be determined since no significant degradation occurred. Accumulative volatiles amounted to 1.95% of the dosed radioactivity at the end of the study.

4.3.5 Aerobic Aquatic Metabolism

Data from this study also indicate that ^{14}C-DDAC is stable to microbial degradation (94). Microbially active pond water and sediment treated to a nominal concentration of 10 ppm ^{14}C-DDAC were incubated for one year under dark, aerobic conditions at 25°C. Flooded sediment samples collected at 0, 1, 3, 7, 14, 31, 61, 92, 123, 182, 273, and 365 days after dosing were extracted and analyzed for ^{14}C-DDAC. The water layers from the flooded sediment samples were also analyzed for ^{14}C-DDAC.

Following the incubation period, a mean of 88.5% of the dosed radioactivity remained as parent compound. A half-life of 8,365 days (~23 years) was calculated, based on first-order degradation. Again, an accurate half-life could not be determined because of the low level of degradation. At the end of the study, accumulative volatiles amounted to 4.51% of the dosed radioactivity.

4.3.6 Anaerobic Aquatic Metabolism

This study again found ^{14}C-DDAC to be stable to microbial degradation (95). Microbially active water and sediment treated to a nominal concentration of 10 ppm ^{14}C-DDAC were incubated under dark, anaerobic conditions at 25°C for one year. Flooded sediment samples collected at 0, 1, 3, 7, 14, 31, 61, 92, 123, 182, 273, and 365 days after dosing were analyzed for ^{14}C-DDAC. The water layer from the flooded sediment samples was also analyzed.

Following the incubation period, a mean of 90.8% of the dosed radioactivity remained as parent compound. A half-life of 6,218 days (~17 years) was calculated, based on first-order degradation. Again, this half-life is an estimate and not an accurate measure since no significant degradation occurred during the study.

4.3.7 Leaching from Wood

Leaching of DDAC from treated wood has been tested using F-2, Timbercote II, and NP-1. In the first F-2 study (20), significant quantities of borate and DDAC

(780 mg/m² and 112 mg/m², respectively) were lost from the surface of treated wood under conditions of simulated rainfall. Unfortunately, potential levels of the chemical in stormwater and the detection limits for this experiment were not reported.

In the second F-2 study (61), unseasoned hem-fir lumber was spray-treated with a 14% active ingredients F-2 solution (~6% DDAC). A rotary lawn sprinkler provided a constant and uniform rainfall of about 5.5 mm/hr to each of three packages. Leachates were collected at the tilted end of each package from 30 minutes after the onset of sprinkling, to completion of the study after eight days.

Concentrations of DDAC measured in the leachates fell rapidly from an initial level of 48 ppm to below 10 ppm after 12 hours, and to about 6 ppm after 24 hours. Keeping the package protected for 24 hours before simulated rainfall greatly reduced the initial rates of leaching to about 15 ppm, but final leaching rates after 48 hours were similar to those from the unprotected package. After 48 hours of rainfall (264 mm), about 6.4% of the DDAC originally applied had been leached from the lumber surfaces of both the unprotected package and the package stored under cover for 24 hours before leaching.

The Timbercote II study (62) measured DDAC concentrations in leachate from two treated and two untreated packages of lumber after seven rainfall events over 18 days. Artificial rainfall was not used for this study to avoid the possibility of chlorine contamination from tap water in the leachate samples. Results indicate that DDAC leached from Timbercote II treated lumber: DDAC concentrations of 73.2 and 65.8 ppm were recorded during the first two leaching cycles. After the seventh leaching cycle, a DDAC concentration of 6 ppm was measured in the leachate.

An NP-1 leaching study done by government and industry has also been completed (92). However, a final report was not available to the Ministry at the time of finalization of this document, so results cannot be summarized here.

5.0 PHARMACOKINETICS

One preliminary and three large-scale pharmacokinetic experiments on rats have been performed. These studies determined absorption, distribution, metabolism, and excretion patterns following the administration of carbon-14 labelled DDAC (23). The preliminary experiment collected data on the amount of ^{14}C eliminated in the expired air following acute oral administration of ^{14}C-DDAC. Results of this experiment and results of administering DDAC as a single low oral dose, as a repeated low oral dose, or as a single high oral dose are summarized below.

In the preliminary experiment, four rats (2 male, 2 female) were fasted for 18 hours, then administered 5 mg/kg ^{14}C-DDAC. Animals were immediately placed in individual glass metabolism cages, and expired CO_2 was collected and analyzed for radioactivity.

Eighteen hour fasted rats (5 male, 5 female) were used in each of the large-scale experiments. Animals were dosed with either 5 mg ^{14}C-DDAC/kg (low dose groups), or with 50 mg/kg (high dose group). Rats in the repeated low oral dose experiment were fed diets containing 34 ppm DDAC for 14 days prior to administration of a single dose of 5 mg/kg ^{14}C-DDAC. For all groups, urine and feces were collected at predetermined intervals and subsequently analysed for ^{14}C content. Seven days after dose administration, rats were euthanized and selected tissues and organs were analyzed for radioactivity.

5.1 Absorption, Transport, and Distribution of DDAC

Because DDAC is highly ionic, it is not expected to be well absorbed from the gastrointestinal tract after oral administration. Excretion results (see below) are consistent with this expectation. Transport characteristics of the chemical were not documented, but tissue and carcass analysis revealed that only a negligible amount (0.003-0.675%) of dosed radioactivity remained in the body after 7 days.

5.2 Metabolism and Excretion of DDAC

The preliminary study (23) showed that little or no radioactivity (0.041-0.054% of dose) was excreted as $^{14}CO_2$ during the 24 hours following oral administration of ^{14}C-DDAC. This indicates that the ^{14}C radiolabel was in a stable portion of the DDAC molecule.

In all of the large-scale experiments, 89-99% of the recovered radioactivity was found in the feces, and less than 2.5% was found in the urine. This finding is consistent with the predicted low absorption of the chemical after oral administration. The pattern of excretion of radioactivity in male and female rats in all dosage groups was similar.

A further study to determine the metabolic profile of ^{14}C residues in fecal samples involved dosing 5 male and 5 female rats with 50 mg ^{14}C-DDAC/kg (24). Following extraction and clean-up procedures, the metabolic profile of ^{14}C-residues in the feces was determined and compared with that of animals in the large-scale studies (23). The pattern of excretion was again similar between the sexes, although a dose-dependent metabolism was observed in females: more parent compound was metabolized in the single low oral dose than in the single high oral dose.

The metabolic process for DDAC in the rat was found to involve oxidation of the decyl sidechain to a variety of oxidative products. Evidence seems to favour initial hydroxylation of the carbon next to the terminal carbon, followed by formation of a hydroxyketone. The four major metabolites found in this study were more polar and presumed to be less toxic than the parent compound, although their chemical structures were not definitively identified.

5.3 Placental and Milk Transfer of DDAC

No data on placental or milk transfer were available for review.

5.4 Pharmacokinetics of DDAI

A study on the dermal and gastrointestinal absorption of ^{3}H-labelled didecyldimethylammonium iodide (DDAI) in rats was also located (84). DDAI is similar to DDAC, but the chloride ion is replaced by an iodide ion. Chemical behaviours of the two compounds are expected to be similar (84). The results indicate that the test compound does not readily penetrate cell membranes and that it is very stable and does not undergo degradation on the skin or in the stomach. Analysis of urine metabolites revealed that DDAI metabolism probably proceeds by oxidation and conjugation reactions analogous to the degradation of the fatty acids by B-oxidation. No $^{14}CO_2$ was detected in expired air, thus complete oxidation and N-dealkylation of the decyl group is not expected to occur.

6.0 TOXICOLOGICAL EFFECTS

6.1 Human Toxicity

Although the mammalian toxicity of quaternary ammonium compounds is not well established, several human fatalities have been ascribed to them (36). One source (1) listed a human oral LD50 of 450 mg DDAC/kg, and an acute dermal LD50 of 4300 mg/kg. These approximate human oral and dermal LD50 estimates are believed to be based on an extrapolation from undisclosed animal studies, although this was not stated in the source. A review of 10 human fatalities involving QACs concluded that the nature of the human toxic response varies widely with the dose and concentration of the substance, as well as with the route of administration and survival time of the victim (37).

6.2 Mammalian Toxicity

The following toxicity data are for various formulations of DDAC, as listed in Appendix B. All reported data have been converted to 100% active ingredient (AI), i.e. 100% DDAC, although it must be emphasized that the listed formulations were tested. Toxicity ratings, based on 100% active ingredients, follow each oral and dermal toxicity value and reference, according to the table in Appendix C.

a) Acute Oral LD50:

Formulation	Species	Reported LD50	Converted (100% AI)	Toxicity
Bardac 2250	Rat	450 mg/kg (73)	225 mg/kg	4
Bardac 2280	Rat	450 mg/kg (2)	360 mg/kg	4
Timbercote II	Rat	1800 mg/kg (69)	360 mg/kg	4
F-2 Concentrate	Rat (males)	3500 mg/kg (68)	399 mg/kg	4
F-2 Concentrate	Rat (females)	2850 mg/kg (68)	325 mg/kg	4
100% DDAC	Rat	84 mg/kg (25)	84 mg/kg	4
100 % DDAC	Mouse	268 mg/kg (25)	268 mg/kg	4
5-25% DDAC	Rat	1190 mg/kg (38)	59.5-297.5 mg/kg	4

b) Acute Dermal LD50:

Formulation	Species	Reported LD50	Converted (100% AI)	Toxicity
Bardac 2280	Rabbit	>2000 mg/kg (2)	>1600 mg/kg	3
Bardac 2250/80	Rabbit	4350 mg/kg (80)	2175-3480 mg/kg	3
Bardac 2250/80	Rabbit (abraded skin)	3500 mg/kg (80)	1750-2800 mg/kg	3
80% DDAC	Rabbit	3342 mg/kg (64)	2674 mg/kg	3
Timbercote II	Rabbit	13,368 mg/kg (69)	2674 mg/kg	3
F-2 Concentrate	Rat	>2000 mg/kg (68)	>228 mg/kg	4

A subchronic dermal toxicity study in rats (16) involved application of 0, 0.1, 0.3 and 0.6% (w/w) DDAC solutions to the clipped backs of animals for 5 days per week over 13 weeks. The sites of administration were occluded for at least 6 hours on each day of dosing, after which time the dressings were removed and the application site rinsed with tap water and blotted dry. All solutions were administered at a constant volume of 2.0 ml/kg/day. The three concentrations therefore corresponded to dosage levels of 2, 6, and 12 mg/kg/day.

No treatment-related changes in clinical signs, food consumption, body weights, weight gain, ophthalmic parameters, hematology, clinical chemistry, gross pathology, or histopathology were observed. Mild skin irritation at the treatment site was observed in most animals at the 12 mg/kg/day level, in a few animals at the 6 mg/kg/day level, and in one female at the 2 mg/kg level.

c) Intraperitoneal LD50:

100% DDAC	Rat	45 mg/kg (25)
100% DDAC	Mouse	11 mg/kg (25)
100% DDAC	Guinea Pig	7 mg/kg (25) (LDLo*)

*Lowest published lethal dose

d) Intravenous LD50:

0.5 - 1.0% solution	Mouse	27 mg/kg (38)

f) Primary Skin Irritation: Rabbit Severely irritating (2)

In an older study (67), a single application of technical grade (50%) DDAC to intact and abraded rabbits' skin caused severe erythema and edema after 24 and 72 hours on intact skin, and on skin surrounding the abraded area. Additional studies with the same product ("Aliquat 203") found that a 10% solution (5% DDAC) gave erythema, edema, and slight necrosis on rabbit skin (67). The non-irritating concentration was 0.01% (0.005% DDAC).

g) Sensitization:	Humans	Nonsensitizer (38)
	Guinea pigs	Nonsensitizer (68, 81)

h) Acute Inhalation LC50:

No studies were available for evaluation.

i) Feeding Studies:

A subchronic range finding study on mice involved dosing 15 animals/sex/group with 0, 100, 300, 600, 1000, or 3000 ppm DDAC for 89 days (males) or 90 days (females) (26). For the lowest four dose groups, these doses correspond respectively to mean intake levels of approximately 18, 52, 107, and 182 mg/kg for males, and 23, 68, 134, and 224 mg/kg for females. High mortality in the 3000 ppm groups prohibited calculation of daily intakes.

Treatment of mice with 3000 ppm DDAC in the diet for several days resulted in virtually 100% mortality in both sexes, with only one male surviving to termination of the study. Death was attributed to treatment-related severe wasting and dehydration resulting from gastrointestinal effects.

Treatment with 1000 ppm DDAC produced a 5% decrease in body weight in males with associated decreases in body weight gain. Similar depressed body weight in the females from this group was assumed to be related to DDAC exposure. No other changes were observed in males or females in the other dose groups. A clear definition of a maximally tolerated dose (MTD) for this experiment was not calculated due to the steep dose-response from virtually 100% mortality for mice in the 3000 ppm group to minimal body weight effects in the 1000 ppm group. The No Observed Effect Level (NOEL) for this experiment was 600 ppm (107-134 mg/kg/day).

In a similar 90 day subchronic oral toxicity study (15), Sprague-Dawley rats (15 rats/sex/dose) were exposed to DDAC at mean intake levels of 6, 18, 37, and 61 mg/kg/day for males, and 8, 22, 44, and 74 mg/kg/day for females (i.e. 100, 300, 600, and 1000 ppm groups, respectively). High mortality in the 3000 ppm group prohibited calculation of mean daily intakes.

Dietary exposure to 3000 ppm DDAC resulted in 80% mortality in both sexes. The three rats of each sex of this group that survived to the end of the experiment exhibited markedly reduced body weights, fluid- or gas-filled intestines at necropsy, and inflammation of the beginning of the large intestine (typhlitis). Pathological changes in clinical chemistry included decreased serum glucose and protein concentrations in both sexes, decreased albumin and globulin concentrations in females, and increased erythrocyte count and hemoglobin and hematocrit concentrations in males. These findings were considered to be related to the debilitated condition of the animals and/or the gastrointestinal lesions resulting from treatment. Experimentally induced fatalities were thought to result from gastrointestinal blockage and shock.

Administration of 1000 ppm or less of DDAC resulted in no treatment-related effects. The NOEL for DDAC in this strain of rat was therefore concluded to be 61-74 mg/kg/day.

In a recently completed chronic toxicity study (96), beagle dogs were dosed orally with 0, 3, 10, or 30 mg DDAC/kg/day (4/sex/group) for 52 weeks. During the first four and a half weeks of the study, several dogs in the 30 mg/kg/day dose group showed potentially life threatening decreases in body weight and food consumption. The dose was therefore decreased to 20 mg/kg/day. In some cases, depressions in weight and food consumption were so severe that the dogs in this group were removed from treatment completely during study days 31-36, and then reinstated at the 20 mg/kg/day dose level.

Results show that chronic administration of 3 to 20 mg DDAC/kg/day was not associated with mortality, changes in organ weights, gross pathological findings, ophthalmoscopic changes, or microscopic changes in selected organs and tissues. The 20 mg/kg/day dose was associated with decreases in mean erythrocyte counts; hemoglobin and hematocrit values; and mean total cholesterol, total protein, and albumin values. The 20 and 10 mg/kg/day doses were associated with an increased incidence of emesis, salivation, and soft/mucoid/liquid feces as compared to controls (96). The NOEL for systemic toxicity was considered to be 10 mg/kg/day.

In a chronic dietary toxicity/oncogenicity study (97), Sprague-Dawley rats received DDAC in the diet at concentrations of 0, 300, 750, or 1500 ppm for at least 104 weeks. These doses corresponded to approximate mean DDAC intakes of 13, 32, and 64 mg/kg/day for males, and 16, 41, and 83 mg/kg/day for females.

Treatment-related decreases in body weight and food consumption in both males and females were observed in the 1500 ppm group. In addition, possible treatment-related microscopic changes including hyperplasia of bile ducts in female rats and changes in mesenteric lymph nodes in male and female rats related to blood in the sinuses were observed in the 1500 ppm treatment group. No treatment-related effects were seen in the type or incidence of clinical signs, survival, palpable masses, clinical pathology, organ weights, gross anatomic pathology, or ophthalmology. The NOEL for toxicity was considered to be 750 ppm. DDAC was not considered to be oncogenic under the conditions of this study.

A similar dietary oncogenicity study using CD-1 mice involved dosing animals with 0, 100, 500, or 1000 ppm DDAC for at least 78 weeks (98). Approximate mean intake levels were 15, 76.3, and 155.5 mg/kg/day for males, and 18.6, 93.1, and 193.1 mg/kg/day for females.

Treatment-related findings included decreased body weights and body weight gains in both males and females from the 1000 ppm groups. There were no treatment-related clinical signs of toxicity, increases in palpable masses, changes in food consumption, differences in organ weights or observations at necropsy, or differences in histopathological findings. The NOEL for this study was considered to be 500 ppm. DDAC was not considered to be carcinogenic under the conditions of this study.

For sake of completeness, a study is summarized here which the federal government of Canada (2) has indicated was seriously flawed. The government has stated the study is of little value in assessing the toxicological consequences of short term exposure, but reasons for dissatisfaction were not stated.

Dogs given doses of 5, 15, or 50 mg/kg (4 dogs/sex/group) of Bardac 22 (50% DDAC, 20% isopropanol, 30% water) for 13 weeks exhibited no toxic effects in any dose group (3). Behaviour, hematological, biochemical, urological, and pathological findings were within normal ranges throughout the study. The only treatment-correlated response found for any parameter was a slight weight depression in dogs given 50 mg/kg. A NOEL was not stated, but no toxic or pharmacologic effects were observed in any dose group.

6.3 Aquatic Toxicity

The following aquatic toxicity data are for various formulations of DDAC, as listed in Appendix B. All reported data have been converted to 100% active ingredient (AI), i.e. 100% DDAC, although less potent formulations may have been tested. Types of tests are indicated by: (f) - flow through bioassay, (s) - static bioassay, or (u) - unspecified bioassay. Toxicity ratings follow each 100% AI 96 hour toxicity value and reference, according to the table in Appendix D.

24 hr LC50:

Concentration	Species	Reported 24 hr LC50	Converted(100% AI)
100% DDAC	Bluegill Sunfish	(u) 0.60 ppm (46)	0.60 ppm

Bardac 22	Rainbow Trout	(u) 1.25 ppm (70,75)	0.63 ppm	
48 hr LC50:				
Concentration	Species	Reported 24 hr LC50	Converted(100% AI)	
Bardac 22	Catfish	(s) 4.8 ppm (71)	2.4 ppm	
Bardac 22	Bluegill sunfish	(s) 0.75 ppm (71)	0.38 ppm	
100% DDAC	Bluegill sunfish	(u) 0.30 ppm (46)	0.30 ppm	
Bardac 22	Rainbow Trout	(u) 1.18 ppm (75	0.59 ppm	
Bardac 22	Guppies	(u) 1.9 ppm (47)	0.95 ppm	
100% DDAC	*Daphnia magna*	(s) 0.094 ppm (10)	0.094 ppm	
96hr LC50:				
Concentration	Species	Reported 24 hr LC50	Converted(100% AI)	Toxicity
Bardac 22	Catfish	(s) 2.6 ppm (71)	1.3 ppm	3
100% DDAC	Bluegill sunfish	(s) 0.32 ppm (11)	0.32 ppm	4
Bardac 22	Bluegill sunfish	(s) 0.59 ppm (71)	0.295 ppm	4
Bardac 22	Bluegill sunfish	(u) 0.54 ppm (44)	0.27 ppm	4
Bardac 2280	Rainbow Trout	(s) 0.880 ppm (41, 74)	0.704 ppm	4
Bardac 22	Rainbow Trout	(u) 1.1 ppm (45)	0.55 ppm	4
Timbercote II	Rainbow Trout	(s) 12.4 ppm (41)	2.48 ppm	3
F-2	Rainbow Trout	(s) 3.9 ppm (41)	0.44 ppm	4
F-2	Rainbow Trout	(s) 4.6 ppm (42)	0.52 ppm	4
assumed 100%	Rainbow Trout	(u) 1.24 ppm (2)	1.24 ppm	3
assumed 100%	Rainbow Trout	(u) 2.81 ppm (41)	2.81 ppm	3
100% DDAC	Coho Salmon	(s) 1.0 ppm (9)	1.0 ppm	3
F-2	Coho Salmon	(s) 5.9 ppm (43)	0.67 ppm	4
F-2	Chinook Salmon	(s) 3.2 ppm (64)	0.36 ppm	4
Bardac 22	Guppies	(u) 1.2 ppm (44, 47)	0.6 ppm	4
100% DDAC	Mysid Shrimp	(s) 0.069 ppm (8)	0.069 ppm	5
NOEC*	Species	100% DDAC		
	Bluegill Sunfish	(s) 0.10 ppm (11)		
	Coho Salmon	(s) 0.59 ppm (9)		
	Mysid Shrimp	(s) 0.052 ppm (8)		
	Daphnia magna	(s) 0.074 ppm (10)		

* No Observed Effect Concentration

6.3.1 Bioconcentration

A bioconcentration study on Bluegill sunfish (*Lepomis macrochirus*) involved continuous exposure of fish to 59 ug of ^{14}C-DDAC/L of water for 28 days (27). This treatment was followed by an 18 day depuration period in which 40 fish were transferred to flowing, uncontaminated water. Radiometric analyses of water and selected fish tissues revealed that the concentration of ^{14}C-residues in nonedible, edible, and whole body tissues reached a steady state by day ten. Mean steady state bioconcentration factors for these tissues were 140x, 38x, and 81x, respectively.

Elimination of ^{14}C-residues from the selected tissue portions and consequently from whole body tissue was measured during the depuration period. Half-life of residues present on the final day of DDAC exposure was determined to be between 7 and 14 days of depuration. By day 14 of the depuration period, ^{14}C-residue concentrations present on the last day of exposure in the nonedible, edible, and whole fish tissues had been reduced by 71%, 57%, and 67%, respectively, based on tissue analysis of five fish. At the end of the depuration period (18 days), percentages eliminated for nonedible, edible, and whole body tissue were 66%, 38%, and 56%, respectively, compared to concentrations present at the beginning of depuration. Percent elimination appeared somewhat lower than at day 14 due to relatively high ^{14}C-residues in one of the fish sampled.

Skin tissue analysis after 28 days exposure showed ^{14}C levels approximately 2 to 6 times higher than those in edible tissues, indicating that there is significant binding of DDAC to the skin and scales of exposed bluegill sunfish. Based upon the short amount of time it took DDAC to reach steady-state and to depurate from tissues, along with the relatively low bioconcentration factor in edible tissues, DDAC would not be expected to bioconcentrate in fish tissues.

6.4 Avian Toxicity

<u>Acute Oral LD50:</u>		
Bardac 22?	Mallard Ducks	3300 mg/kg (70)
<u>8 Day Oral LC50:</u>		
Bardac 22	Bobwhite Quail	1950 ppm* (77)
100% DDAC	Bobwhite Quail	975 ppm (from 77)
Bardac 22	Mallard Duck	>3500 ppm* (77)
100% DDAC	Mallard Duck	>1750 ppm (from 77)

*mg/kg unspecified

6.5 Phytotoxicity

The toxic effect of QACs on the unicellular green alga *Chlorella*, and on a duckweed *Spirodela oligorhiza* has been investigated (48). In general, all types of QACs were strongly phytotoxic, with suppressed plant growth evident at concentrations above 10^{-5} M (approximately 3 to 5 ppm). Bardac 22 at 3 to 5 ppm suppressed plant growth in both species after 3 days. In duckweed, sublethal levels of QACs caused a yellowing or browning of the frond margins and the production of smaller sized fronds. In *Chlorella*, the size, shape, and internal organization of the cell were affected; death appeared to be due to disruption of chloroplast structure.

6.6 Comparative Toxicity

A comparison of some toxicity values for various antisapstain chemicals is shown in Table 1. From this table it is evident that, of the non-chlorophenol antisapstain chemicals, DDAC is the most toxic orally. However, it is one of the least aquatically toxic compounds. Consideration of the aquatic toxicity of DDAC is important since much of the stormwater effluent from lumber mills is discharged into rivers, lakes, or oceans, thereby exposing aquatic species to the chemicals used. Chemicals from leaching, spills, and other discharges also find their way into groundwater, and other bodies of water.

7.0 CARCINOGENICITY

Two carcinogenicity studies have been submitted by the manufacturer. In the first study (97), Sprague-Dawley rats received DDAC in the diet at concentrations of 0, 300, 750, or 1500 ppm for at least 104 weeks. These doses corresponded to approximate mean DDAC intakes of 13, 32, and 64 mg/kg/day for males, and 16, 41, and 83 mg/kg/day for females. DDAC was not considered to be oncogenic under the conditions of this study.

In the second study, CD-1 mice received 0, 100, 500, or 1000 ppm of DDAC in the diet for at least 78 weeks (98). Approximate mean intake levels were 15, 76.3, and 155.5 mg/kg/day for males, and 18.6, 93.1, and 193.1 mg/kg/day for females. Again, DDAC was not considered to be carcinogenic under the conditions of this study.

Presently, DDAC is not listed as a carcinogen by the National Toxicology Program, the International Agency for Research on Cancer, the Occupational Safety and Health Administration (40), or the Registry of Toxic Effects of Chemical Substances (RTECS).

8.0 - MUTAGENICITY

Several studies evaluating the mutagenicity of DDAC have all given negative results. In the *in vitro* rat primary hepatocyte Unscheduled DNA Synthesis (UDS) assay (18), DDAC did not induce significant increases in UDS. Freshly prepared hepatocytes were exposed to concentrations of the chemical ranging from 0.05 ug/ml to 10 ug/ml. Concentrations ranging from 0.05 ug/ml to 2.00 ug/ml were selected for analysis of nuclear labelling and represented a good range of toxicity in both trials. None of the criteria used to indicate a UDS response was approached by the test material and no dose-related response was observed. The test material was therefore evaluated as inactive in this assay.

In a second mutation assay (19), the ability of 80% DDAC to induce forward mutations at the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus in Chinese hamster ovary (CHO) cells was evaluated. Testing was performed with and without S9 metabolic activation. Mutant frequencies of all cultures treated with DDAC varied randomly with dose within the range acceptable for vehicle control mutant frequencies. Several random cultures did achieve statistical significance but were apparently due to normal assay variation and to vehicle control mutant frequencies that were on the lower end of the normal range. DDAC was therefore considered negative for mutagenic activity under the conditions of this assay.

Another study investigated the ability of DDAC to induce chromosomal aberrations in CHO's *in vitro* (72). Doses of 2, 4, 8, and 16 ug Bardac 22/ml were tested with activation, while doses of 1, 2, 4, and 8 ug/ml were tested without activation. Results indicated that Bardac 22 is not clastogenic in CHO cells *in vitro*, with or without metabolic activation.

In a *Salmonella typhimurium*/Ames assay, no mutagenic activity was observed when Bardac 22 was tested in strains TA 1535, TA 1537, TA 1538, TA 98, and TA 100 (82). Results were negative with and without metabolic activation. A bone marrow cytogenetic assay in rats treated with 600 mg/kg also gave negative results (1, 2).

One *in vivo* cytogenetic test assessed the effect of Bardac 22 on the incidence of chromosomal damage in rats (83). Rats were treated with the test compound by gastric intubation at a dose of 600 mg/kg bodyweight, then sacrificed at 6, 24, or 48 hours post dose. Results showed that Bardac 22 did not cause any statistically significant increases in the proportion of cells showing chromosomal damage at any of the three time points.

9.0 TERATOGENICITY AND REPRODUCTIVE EFFECTS

Two developmental toxicity studies, results of one teratogenicity study, and a two-generation reproduction study were located. In the first developmental toxicity study (28), sixteen mated New Zealand female white rabbits per dosage group were administered 0.0, 1.0, 3.0, or 10.0 mg/kg/day of DDAC by gavage at gestational days (gd) 6 through 18. The vehicle was deionized water.

Four of 16 does in the highest dose group died prior to gd 13. One doe at 10 mg/kg and two does at 1.0 mg/kg delivered early and were removed from the study. No females aborted. Maternal toxicity, including mortality, was evident at 10 mg/kg. Nonlethal indications of maternal toxicity were evident at 3 and 10 mg/kg, as evidenced by reduced weight gain and clinical signs during the treatment period. Developmental toxicity, including increased incidence of fetal mortality and reduced fetal body weight per litter, were observed only at the highest dose. No teratogenicity was observed at any dose employed. The NOEL for maternal toxicity was set at 1.0 mg/kg/day, and the NOEL for developmental toxicity was set at 3.0 mg/kg/day.

The second developmental toxicity study involved dosing timed-pregnant Sprague-Dawley rats with DDAC on gestational days 6 through 15 (31). Twenty-five females per group received 1, 10, or 20 mg/kg/day by gavage.

No females died, aborted, delivered early, or were removed early from the study. Maternal toxicity was indicated at 10 and 20 mg/kg/day by characteristic clinical signs of audible respiration. Reductions in body weight and food consumption were also observed at 20 mg/kg/day during the treatment period. No evidence of developmental toxicity including teratogenicity was observed at any dose employed. The NOEL for maternal toxicity was 1.0 mg/kg/day. The NOEL for developmental toxicity was at least 20 mg/kg/day.

In female rats receiving 10, 25, or 50 mg/kg of Bardac 20, Bardac 22, or Bardac LF (percent DDAC unspecified) by oral gavage on days 6 to 15 of gestation, no teratogenic effects were observed (76). However, all formulations did cause several females to resorb one or more fetuses at the 50 mg/kg level.

A reproduction study (32) using Sprague-Dawley rats involved dietary administration of DDAC at target dosage levels of 0, 300, 750, or 1500 ppm for two generations. Dose levels in terms of mg/kg/day decreased throughout the study as animal body weight increased, and varied within and between dose groups and generations, so are not reported here.

A total of 28 males and 28 females were evaluated at each dose level. Animals were exposed to DDAC for 10 weeks prior to mating, and each of the two generations produced two litters. The original rats, called the F0 generation, were randomly paired within dose groups and mated over a three-week period to produce the F1A generation. Exposures continued through mating, gestation, parturition, and lactation. At least 10 days after weaning the F1A litters, F0 parents were mated in different male-female pairings, within dose groups, to produce the F1B generation. Exposures to DDAC again occurred from mating to lactation. After the F1B animals were weaned, F0 parents were necropsied and high dose and control animals were examined for histopathologic lesions.

Selected F1 parents were exposed to the same concentrations of DDAC as their parents for at least 10 weeks, and were then paired as described above to produce F2A and F2B generations. Mating, gestation, lactation, and necropsy of the F1 parents and selected F2A and F2B pups were performed as outlined above, except that no F2 animals were selected as parents.

Results indicate that continuous exposure to DDAC in the diet for two generations resulted in no adverse reproductive effects. Parental toxicity was observed at 1500 ppm (~112.6 mg/kg/day), limited to body weight reduction, weight gain depression, and decreased food consumption. Postnatal toxicity at 1500 ppm was indicated by reduced pup body weights. The NOEL for both adults and offspring was 750 ppm, indicating no increased risk to offspring in the absence of indications of adult toxicity.

10.0 IMPACTS OF OCCUPATIONAL EXPOSURE

Although DDAC has been used extensively in various applications, no quantitative occupational exposure data were located for any DDAC formulation. However, a review of F-2 concentrate (66) noted that sawmill workers in the mixing room could contact F-2 by splashing on the skin and into the eyes. It was also stated that most workers are potentially exposed to diluted treating solutions, mainly by skin contact while handling treated lumber. Workers near a poorly operating spray box or doing maintenance work on the box could be exposed to spray mist.

Information on human exposure to QACs has been fairly well documented (21). Since all QACs probably produce similar toxic effects (21), these are summarized here. Concentrated aqueous solutions (10% and sometimes less) are primary skin irritants, and concentrations as low as 0.1 to 0.5% are often irritating to conjunctivae and mucous membranes. Percutaneous absorption is probably insignificant.

Information on inhalation toxicity of the chemical was not found. Oral ingestion of strong aqueous solutions (10-20%) commonly produces superficial necrosis of mucous membranes with which they come in contact. Severe corrosion of the upper alimentary tract, and erosion, ulceration, and hemorrhage at the surface of the small intestine have also been observed.

Based on the concentrations involved in the above cases, the use of DDAC in the workplace is potentially hazardous. Inhalation was expected to be the main route of occupational exposure in one study (39), but air monitoring tests in several mills that use DDAC have shown a minimal risk. Because dermal exposure may also be a problem in mills, the use of proper protective clothing, including gloves, boots, and chemical goggles, and following proper chemical procedures are indicated.

An Acceptable Daily Intake (ADI) has been calculated by BC Environment. This value, derived in Appendix E, is 22.4 mg/day for a 70 kg person.

11.0 FOOD USE

DDAC is currently registered for a variety of antimicrobial uses under conditions where contamination of food products is unlikely (2). There are no data available in Health and Welfare Canada files concerning the potential food contamination resulting from the use of treated wood in the construction of food holding containers or storage facilities (2).

12.0 ANALYTICAL METHODS OF DETECTION

Two standard analytical methods for DDAC were supplied by Lonza (33). The first method involves detection of tertiary amines and alkyl chlorides by gas chromatography. The second method involves quantification of these compounds based on their solubility relationships in aqueous and chloroform layers. Detection limits were not stated but it appears that the method is used mainly for quantifying DDAC concentrations in NP-1 working dilutions, and for leachate and F-2 analyses (91).

Another method from Lonza (63) involves preparation of a disulphine blue indicator and its reaction with DDAC to form the disulphine blue-DDAC complex in chloroform. Chloroform solutions are then measured for DDAC levels by UV spectrometry using the absorption maximum at 625 nm for the disulphine blue-DDAC complex. Detection limits were not indicated.

An older method of analysis (35) used to measure DDAC in the range of 2-10% total chlorine involves combustion of the sample in a Parr oxygen bomb, with conversion of all chlorine present to an ionic form. The solution is then titrated to determine total chlorine in the sample.

Photolytic and hydrolytic studies sponsored by the manufacturer (12, 13) used thin layer chromatography (TLC) and liquid scintillation counting to measure ^{14}C-DDAC concentrations in water. Samples were spotted onto TLC plates, and the plates were then eluted in chloroform/methanol/formic acid to a distance of at least 10 cm above the origin. After elution, the plates were analyzed on a radio-TLC plate scanner, to locate the ^{14}C-active chromatographic zones. The detection limit was not given, but was at least 10 mg/L.

A QAC biodegradability study used a colourimetric test and UV spectrophotometry (34). For the colourimetric test, 1 ml of reagent (0.02% bromophenyl blue dye in alkaline water) was added to a 100 ml sample produced by adding 7.5% hydrochloric acid to shake flask samples. The reactant was then extracted with chloroform, read at 450 nm and 460 nm on a colourimeter, and measured for QAC concentration by comparison with standard curves prepared for each compound. Limit of detection for a 100 ml sample was 0.25 mg/L, well below detection limits required for enforcing legislation in British Columbia (29). UV spectrometry involved subjecting refluxed samples to UV analysis at 263 and 268 nm and comparing results to specific standard curves to estimate concentrations.

Finally, a recent method developed by BC Research (87) involves treating field samples with hydrochloric acid, then adding a quaternary ammonium surrogate and extracting with dichloromethane. The raw extract is concentrated and a quaternary ammonium performance standard is added to the final extract volume. The extract is then examined on a gas chromatograph equipped with a nitrogen/phosphorus specific detector (NPD). The detection limit is 0.025 mg/L.

13.0 EXISTING LEGISLATION

In British Columbia, provincial regulations (29) state that, from September 1, 1990 forward, the concentration of DDAC in effluent shall not exceed 700 ug/L. A stormwater effluent standard is derived in Appendix F.

Provincial regulations also stipulate that the rate of emissions to the air from chemical spray booth stacks is not legally permitted to exceed 7.0 mg DDAC/second. A derivation of an interim emission standard is shown in Appendix G. No other standards were located.

14.0 CONCLUSION

The use of DDAC in the lumber industry has come about relatively recently, but the compound has a long history of use in other areas. Thus, the toxicological and environmental impact database for DDAC is extensive. Several long-term toxicity, carcinogenicity, reproduction, and developmental toxicity studies have recently been completed, as have environmental degradation studies. These studies answer some questions in terms of its use as an antisapstain chemical.

In laboratory studies, DDAC has been shown to be hydrolytically and photolytically stable. In studies involving wood treatment, DDAC levels as high as 76 ppm have been found in the initial leachates. The concentration of DDAC in later leachates are in the 6 ppm range. These data indicate that there is a potential for significant quantities to enter the environment. Soil adsorption/desorption studies have shown that DDAC is relatively immobile in soil, suggesting that there is little likelihood of ground water contamination from surface soil contamination. The data regarding microbial degradation of DDAC indicate that both the concentration of DDAC, and the type or quantity of microbial organisms initially present are important factors in determining the ultimate fate of DDAC in soil or sediment.

DDAC is moderately toxic to very toxic to mammals, depending on route of administration. It appears to be excreted rapidly, with only low levels remaining in tissues after one week. In terms of aquatic exposure, DDAC is generally moderately to very toxic to fish species. It has been shown to be highly toxic to an alga and to a duckweed, but implications of this toxicity are unknown.

For workers exposed to DDAC or its formulations, the main hazard appears to be its potential to cause severe skin and eye irritation. Importantly, DDAC has not been shown to be mutagenic, carcinogenic, or teratogenic in several laboratory studies. However, further exposure studies should be done to assess the potential occupational impacts of the compound and its formulations.

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Table 1: A comparison of toxicity values of antisapstain chemicals

	Oral LD50* Rat - mg/kg	Dermal LD50* Rabbit - mg/kg	Aquatic 96hr LC50* Fish species**-ppm
DDAC	84[25]	>1,600[2]	0.44[41] Bluegills 0.27[44]
IPBC	1,426[90]	>1,940[90]	0.065[90]
TCMTB	360[56]	324[56]	0.017[56] Chinook 0.015[55]
Copper-8	702[5]	>1,960[5]	0.00016[6]
Sodium carbonate	4,000[56]	not avail.	100[56]
Sodium borate	2,660[56]	>2000[56]	377[56]
NaTCP	210[57]	270[57]	0.3-0.13[57]
NaPCP	71[50]	250[51]	0.048[52] Coho Salmon 0.032[54]
PCP	27[51]	39[50]	0.044[53] Bluegills 0.020[53]

*Values quoted are the lowest measured for each species, and are based on 100% active ingredients, although less potent formulations may have been tested.

**Fish species is Rainbow trout unless otherwise noted.

APPENDIX A

DATABASES SEARCHED FOR INFORMATION ON DDAC

The following computerized databases were searched for information on DDAC:

CA Search
Toxline
Toxlit
AQUIRE
Medline
RTECS
CCOHS

APPENDIX B

PRODUCTS CONTAINING DDAC, AND THEIR MANUFACTURERS

PRODUCT	%DDAC	MANUFACTURER
Bardac 22/2250	50%	Lonza, Inc., Fair Lawn, NJ
Bardac 2280	80%	Lonza, Inc., Fair Lawn, NJ
NP-1	64.8%	Kop-Coat Inc., Pittsburgh, PA
Timbercote II	20%	Napier Pacific Industries Inc. Surrey, BC
F-2	11.4%	Walker Brothers, Burnaby, BC
Ecobrite III	2%	Canfor, Vancouver, BC

APPENDIX C

MAMMALIAN LETHAL TOXICITY CLASSES FOR CHEMICAL COMPOUNDS*

Toxicity Rating	Commonly Used Term	Oral/Dermal** (mg/kg)	Inhalation‡ (ppm-mg/L)
1	Practically Nontoxic	>15,000	>200
2	Slightly Toxic	5,000-15,000	20-200
3	Moderately Toxic	500-5,000	2-20
4	Very Toxic	50-500	0.2-2
5	Extremely Toxic	5-50	0.02-0.2
6	Ultra Toxic	<5	<0.02

*Toxicity ratings adapted from references 21, 85, and 4.

**Index: acute oral or dermal LD50.

‡Index: LC50 - four hour inhalation exposure.

APPENDIX D

AQUATIC LETHAL TOXICITY CLASSES FOR CHEMICAL COMPOUNDS*

Toxicity Rating	Commonly Used Term	Exposure Conc.** (ppm - mg/L)
1	Practically Nontoxic	>100
2	Slightly Toxic	10 to 100
3	Moderately Toxic	1 to 10
4	Very Toxic	0.1 to 1
5	Extremely Toxic	0.01 to 0.1
6	Ultra Toxic	<0.01

*Toxicity ratings adapted in consultation with reference 86.

**Index: 96 hour LC50 or EC50.

APPENDIX E

Calculation of an Acceptable Daily Intake (ADI) of DDAC for Humans

Following a method used by Fox (58), an ADI may be derived for humans based on the 32 mg/kg/day NOEL in male rats in the 104 week chronic dietary toxicity/oncogenicity study (97):

<u>Calculation of human ADI based on rat NOEL</u>

a) NOEL from chronic rat: 32 mg/kg/day (male rats)

a) Safety factor used: 100x

i.e., -100x for conversion of chronic animal to human data

b) Human DDAC ADI: = 32 mg/kg/day/100
= 0.32 mg/kg/day

c) For a 70 kg adult human: = 0.32 mg/kg/day x 70 kg
= 22.4 mg/day ADI